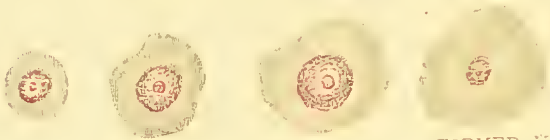
Ce 2.25.

THE CELL:

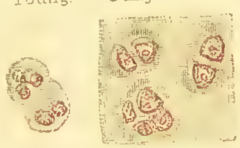
ITS LIVING MATTER — ITS FORMED MATTER.

…WTH AND MULTIPLICATION OF LIVING MA… AND ITS CONV… INTO FORMED MATERIAL.



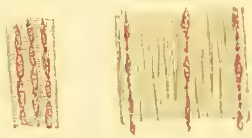
FURTHER PRODUCTION AND ACCUMULATION OF FORMED MATERIAL.

Young. Fully formed



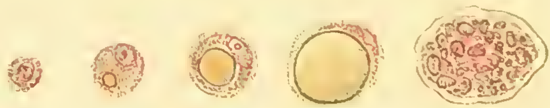
CARTILAGE.

Young. Fully formed.



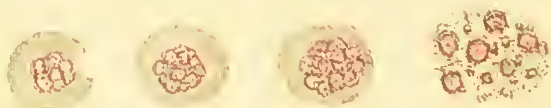
TENDON.

PRODUCTION OF FORMED MATTER: ITS CONVERSION INTO SOLUBLE SUBSTANCES BY OXIDATION—SECRETION.



Fat. Starch.

FORMATION OF SPECIAL SUBSTANCES, OR SECONDARY DEPOSITS, FROM …ERMINAL MATTER.



Increase of … Pus

RESULTS OF INCREASED ACCESS OF PABULUM.

[Ha…

ON THE

STRUCTURE

AND

GROWTH OF THE TISSUES,

AND ON

LIFE.

TEN LECTURES DELIVERED AT

KING'S COLLEGE, LONDON.

BY

LIONEL S. BEALE, M.B., F.R.S.,

FELLOW OF THE ROYAL COLLEGE OF PHYSICIANS; PHYSICIAN TO KING'S COLLEGE HOSPITAL; PROFESSOR OF PHYSIOLOGY AND OF GENERAL AND MORBID ANATOMY IN KING'S COLLEGE, LONDON.
ETC. ETC. ETC.

ROBERT HARDWICKE, PICCADILLY, LONDON.

1865

PREFACE.

THESE Lectures form the first part of my Physiological Course at King's College. They were published in the DUBLIN MEDICAL PRESS, from which Journal they have been reprinted in their present form. The first three Lectures were reported by my friend and former pupil, Mr. Sealy, in the year 1861, but all the rest are of more recent date, and contain some of my latest observations.

The doctrine of the formation of tissue, which was first published in my Lectures at the College of Physicians, is still further elucidated. An attentive examination of the figures in the frontispiece will enable the reader to grasp the main points in this view with very little trouble.

In the last Lecture I have discussed several matters of the greatest interest in connexion with life, and have endeavoured to show that we may distinguish the purely vital actions from the physical and chemical changes taking place in all living organisms. The result of the enquiry is a theory of life which differs in essential particulars from any one hitherto advanced, and is opposed to the modern doctrine that life is but another form or mode of primary energy or motion.

Since my new views were first published in 1860,

they have received further confirmation from many special anatomical investigations, the details of which are given in several memoirs published in the "Philosophical Transactions," the "Proceedings of the Royal Society," the "Quarterly Journal of Microscopical Science," the "British Medical Journal," and my "Archives."

My observations have been already translated into German and Italian. They will therefore be subjected to free discussion and criticism on the Continent.

I am encouraged to hope that with the aid of the new fiftieth of an inch object-glass magnifying more than 2500 linear,* lately made by Messrs. Powell and Lealand, anatomists will be enabled to prosecute investigations into yet more minute detail, and I look forward with the utmost interest to the more minute and careful investigation by other anatomists and physicians of the phenomena accompanying the general morbid changes occurring in the higher animals, feeling sure that by patient and careful research many of the complex pathological doctrines now generally entertained and taught will be much simplified, and the science and practice of Medicine thereby greatly advanced. L. S. B.

61, Grosvenor-street, November, 1864.

* The first fiftieth was completed for me by Messrs. Powell and Lealand, on October 12, 1864. It defines admirably, and admits plenty of light; there is room for focussing over the thin glass cover, and the glass is in all respects a thoroughly useful working objective.

TABLE OF CONTENTS.

LECTURE IV.

LECTURE V.

THE TISSUES.

LECTURE VI.

THE TISSUES (*continued*).

LECTURE VII.

ADIPOSE TISSUE—CARTILAGE.

LECTURE VIII.

BONE.

LECTURE IX.

TEETH.

LECTURE X.

OF LIFE.

ON THE

STRUCTURE AND GROWTH OF TISSUES.

LECTURE I.

Introductory—The Cell and other Theories—The smallest inanimate contrasted with the smallest living particles—Structure of the simplest living organisms—Of the growth of living structures—Of germinal matter and formed material.

GENTLEMEN,—In my Introductory Lecture, after having explained the meaning of the terms Physiology, Biology, and Histology, I enumerated some of the principal subjects which will be considered in this Course of Lectures, and gave an outline of the general arrangement which I proposed to follow. I then pointed out to you that the organism contains many different organs which perform various offices, each of these being composed of a great number of elementary organs exactly resembling each other, and so combined that the work of all is united together. Each *elementary organ* is made up of a variety of textures differing from each other in appearance, structure, and use. For example, in the examination of this

limb which lies before us, we found externally a structure which is well known to you as skin—a tissue not simple in its structure, but made up of several parts, each performing an important *office* or *function*. Beneath this, proceeding from without inwards, another tissue comes into view, very different from the first, called *fat*, or as we shall have to speak of it, *adipose tissue*. Beneath this again, is a firm unyielding, glistening material, spread out like a membrane, admirably adapted for the protection of the more delicate structures beneath. This is composed of a form of *white fibrous tissue*, which is called *Fascia*. Next to this we came to a peculiar tissue, which manifests vital phenomena in a remarkable degree, and the essential property of which is the power of contractility. Ordinarily, this is spoken of as *flesh*, but we call it *muscle*. In connexion with this we noticed certain cords which you will remember I told you were *nerves*, and their office is to bring the muscular substance into relation with the brain, and to convey to it from the brain those voluntary impulses by which its contractions may be excited and governed. Besides these we observed in various parts of the limb certain tubes, and these were of two kinds—the one, with thick, tough, and very elastic walls, and the other with walls less elastic, thinner, and flaccid. Both sets of tubes are in connexion with the heart, but the one set *(arteries)* performs the office of conveying the blood from the heart to the tissues; the other *(veins)*, that of returning the blood from the tissues to the heart. Besides these, there are some very delicate tubes which are called *lymphatics*, in which a colourless fluid passes from the tissues to the venous

circulation. These cannot be seen without being filled with some coloured fluid. Lastly, we noticed the bone, a firm solid substance, in the interior of which is a cavity containing that peculiar modification of adipose tissue known as *medulla* or *marrow*.

I next spoke of *Functions*, and showed you that these may be divided into two great classes, the *animal* and the *organic*, or *vegetative functions*. The one class characteristic of the higher animals only, the other common to all living beings; the former consisting of *Locomotion*, *Innervation*, and *Special Sense*; the latter more widely distributed, and comprising *Digestion*, *Absorption*, *Circulation*, *Respiration*, *Secretion*, *Generation, and Development*, and the *development of Heat*, *Light*, *and Electricity*.

We saw that in the lowest organisms some of the most important vegetative functions are performed through the instrumentality of the general surface; while in man and the higher animals a separate organ is set apart for the performance of each function. Now, in considering these different functions, I shall commence with the functions of organic life in the order in which I have enumerated them, for this seems the most natural mode of arrangement. First of all the food is introduced into the organism, and after being altered by certain preliminary processes, is subjected to digestion, by which it is rendered soluble, and fitted for the next process, that of *Absorption*. By this the nutritive material is taken up and introduced into the blood, and ultimately it becomes itself converted into blood. This will bring us to the consideration of the function of *Circulation*, and as we follow the blood in its

course through the body, our attention will naturally be drawn to the examination of those remaining processes—viz., *Respiration* and *Secretion*, by which great and most important changes are brought about in the condition of the circulating fluid, various substances being separated from it for ulterior uses, or for complete removal from the body. Lastly, we shall consider under the head of *Generation*, the process by which the multiplication of individuals is effected. We shall then consider the functions of animal life.

In discussing each one of these various operations we shall first study the structure of the parts which are concerned, and secondly, examine the function itself.

Before I proceed, however, to the functions, it is necessary that we should consider briefly the nature of the process of *Nutrition—i.e.*, the manner in which the soluble material, which is brought into relation with a living tissue, is taken up by that tissue and incorporated with it; how it becomes converted from an inanimate into a living substance; how the whole organism grows; how tissues increase in size until the adult form is attained; how the waste resulting from action is supplied by the production of new tissue. It is important that you should bear in mind what I have already told you, that living organisms are incessantly undergoing change. New parts are constantly being formed, which grow, arrive at maturity, pass through certain stages of existence, and then having performed their office, die, and are cast away.

It would, indeed, be difficult to answer such questions as these. How does the body grow? how are old parts

removed? and how do inanimate substances become endowed with the peculiar properties of the living tissue with which they are brought into contact? Indeed, many questions of this kind which you would naturally ask, it is not possible in the present state of science to answer conclusively; but by reasoning upon facts obtained by experiment, and upon the observations derived from very minute examination of the tissues with the highest powers of the microscope, inferences which in many cases probably approximate to the truth, have been obtained.

It has not been my custom in former years to trouble you with any very close inquiry into the theories by which observers have endeavoured to explain those phenomena to which I have alluded. Of late, however, these matters have been so freely discussed, not only in scientific books, but even in the current general literature of the day, that I think it very necessary you should be acquainted with some of the arguments for and against the various theories that have been propounded, and that you should have laid before you as simply as possible what is known at the present time of the minute anatomy of the tissues, and of the nature of the changes which go on in the living body. This inquiry has, as I have said, been so brought before the public notice of late, that you will certainly be called upon to give your opinion regarding various points connected with it, and this seems to me a good reason why you should give your attention to the matter; but there is a much stronger reason than this why it should be studied by you—viz., that it is impossible to know anything of the action of the body in health without investigating the

minute changes which go on in the organism. This knowledge forms the foundation of physiological science, and from this point of view the changes taking place in disease can alone be studied with any advantage. It is the natural introduction to the study of medicine. Most important is it that we should investigate the minute changes occurring in the tissues, and endeavour, if possible, to construct a theory which will help us to understand and explain the processes which are incessantly taking place in organized beings.

There is, too, another reason which, I think, ought to induce us to study earnestly, and endeavour to advance every branch of science which bears directly or indirectly upon medicine, and this is the influence which increased knowledge must exert in exposing the false character of the many plausible arguments which are brought forward in favour of various forms of quackery. It is quite clear that if the principles upon which we act were as capable of proof as many of the general doctrines of chemistry, quack dogmas would very soon be exposed; but charlatans know well that the arguments from which our principles of action are deduced cannot be understood by any one ignorant of physical science, while by putting forward false premises, and drawing from these a logical conclusion, they very easily convince even an intelligent well-educated man, who is unable or disinclined to analyze their premises, that there is some reason in their statements. Depend upon it, gentlemen, the only efficient way of opposing the spread of quackery among the public is to encourage the spread of scientific investigation and a love for research among our-

selves, and by this course alone shall we be able to shame those amongst us who are base enough to their profession to support and pamper an impostor or encourage a stupid system of treatment because they have not the courage to offend the prejudices, or oppose the caprices of some self-willed, wealthy, and perhaps influential person. We must oppose the spread of quackery, and endeavour to prevent the harm resulting from it by increased devotion to our profession, by prosecuting researches for the discovery of new truths, or for confirming facts which appear inconclusive, and by unremitting efforts to demonstrate simply and most conclusively the soundness of the fundamental principles of medicine. The skill of the modern chemist exposes the vicious refinements of the most ingenious and subtle poisoner; and in the same way our earnestness and gradually-increasing knowledge of disease must ultimately destroy the influence which unscrupulous charlatans have long exerted upon ignorant persons.

The Cell and other theories.—There are certain points in which all living structures resemble each other—*e.g.*, all spring from preëxisting living structures, and this fact has been proved in the most positive and satisfactory manner by several different kinds of evidence. Again, all living structures are perpetually undergoing change; they grow, are nourished, exist for a time, and ultimately die. They possess the power of assimilating to themselves lifeless matter, and communicating to it the same peculiar properties with which they themselves are endowed; and further, they possess the power of multiplying themselves infinitely—of giving rise to other organisms which inherit similar

properties to those which their progenitors possessed. Various theories have been proposed from time to time with the view of rendering the description of structures as simple and as intelligible as possible, and for the purpose of furnishing us with some general notion of the manner in which tissues are built up in living beings.

The principal of these is that known, as I have no doubt you are aware, as the *Cell-theory.* It was supposed by its originators, Schwann and Schleiden, that all organized beings are developed from cells, and that in those higher creatures whose organisms consist of various tissues differing remarkably from each other in appearance and structure, the differences are caused by certain modifications occurring in the course of the development and growth of the constant structure, the cell. Now, a cell is a small body varying, according to circumstances, in shape and size, but for the most part of a round or oval form, and consisting essentially of a clear transparent membrane in the form of a minute sac closed at all points, and enclosing certain contents. The cell during some period of its life contains another small body, either floating free within it or attached to its internal surface, and this is called a nucleus, and sometimes, though not invariably, in this nucleus may be seen a minute particle which is called a nucleolus; so that if I were to represent roughly the structure of a cell on this board, we shall have a figure somewhat of this sort. Externally a delicate membrane enclosing certain contents, which vary in different cases, but I will represent the cell as it appears in its most distinct form. [Diagram of the cell on the board.]

The *nucleus* is generally darker than the cell contents, but no one has as yet been able to make out any definite structure in it. All that can be said of it when examined by the highest powers is, that it appears granular. Each cell is supposed to be a separate centre of growth, and to increase by attracting to itself materials from without. The manner of cell formation is described briefly as occurring thus: In a perfectly clear fluid, a number of minute points, or, as they are termed, *granules*, make their appearance. Certain of these little particles become aggregated together, and thus a nucleus is formed. Then as this grows by attracting material from around, a membrane is in some way formed around it, and the complete cell is produced. Now, with regard to the multiplication of these cells. This may be accomplished in more ways than one. Reproduction may occur within the interior of the old cell wall, the nucleus of the original cell dividing, and each half appropriating to itself a portion of the cell contents, giving rise to two new cells; and each of these may again subdivide, and so on. But more commonly the process is effected by the division of the original cell, and is said to occur as follows:—A constriction occurs in the wall of the cell, the nucleus at the same time dividing into two parts, and this constriction gradually gets deeper and deeper until the cell is completely separated into two portions, each constituting a new and perfect cell. There is another theory which I must briefly describe to you. It differs materially from the first. It was first propounded by Wolff, and has recently received warm support in this country from Professor Huxley, who has modified

the view in many important particulars. This theory supposes that the organism at the earliest period of its existence consists of a clear semifluid material. Soon certain changes occur in this; spaces or vacuoles which have the appearance of cells are formed. In these, again, nuclei appear. The growth and multiplication of these spaces is effected by changes in the surrounding substance. The division of a space is produced by the surrounding material growing in towards its centre, and so separating the vacuole, cell, or space, into two parts.

The chief difference between the two theories seems to be this, that in the one the cell is the active part, while in the other, the changes that occur are effected by the structure which corresponds to the cell wall, or that which is external to the cell, and known as the *inter-cellular substance.*

Now, in the organism it is certainly true that there are structures composed of bodies resembling cells; but we must bear in mind that there are also tissues to be found whose origin from mere cells it is not so easy to make out. In fibrous fasciæ, tendons, and ligaments, for example, we have a tissue containing here and there nuclei; but it is impossible to demonstrate in it at any period of its existence bodies which might be fairly termed cells. In the structures which apparently correspond to cells in some tissues, there is no cell wall, hence they have been termed *nuclei*, while it is believed that the material, the fibrous tissue in which they lie, is formed altogether independently of these. In the case of many other tissues of the body, accepting for a moment the cell theory as true, it is difficult to con-

ceive how the cells were formed, and to explain how by any changes occurring in cells, the structure which exists could be produced. In some of the tissues, as I have said, the explanations offered by these theories are intelligible enough, but they seem to be exceedingly unsatisfactory when applied to many others, and quite inadequate to explain the changes which have occurred, or to account for the structure which exists, even in tissues closely allied to those composed of bodies like cells.

Let me now ask you to dismiss for the present from your minds all theories, and to consider with me the changes that may be actually seen to take place in the growth of various organisms when examined under the most favourable circumstances by the highest powers of the microscope. We shall, then, attempt to generalize from these particular observations, and it may be, propound some theory which will help us to understand the nature of the processes by which the tissues are built up. In the first place, it is most important that we should examine the most minute inanimate particles and the smallest living particles.

The smallest inanimate particles contrasted with the smallest living particles.—Suppose, then, we take a little inorganic matter of any kind and place it under the microscope. We will take, say, a little of this deposit of phosphate of lime which I have precipitated from a solution of lime by the addition of a soluble salt of phosphoric acid. Now, what do you see on putting this fine precipitate under the microscope? Why, only a number of minute granules or dots possessing no form or structure whatever. Magnify the deposit by the highest powers at your command, and you

will, indeed, increase the size of the particles you saw before, and bring into view others which were previously invisible, but you will still be unable to recognize any appearance of structure. Points they were under moderately high powers, and mere points they remain under the highest magnifying powers we can obtain; but you will observe that certain movements are going on. Each little particle is revolving rapidly and oscillating in the fluid. These movements are termed *molecular*, and were first described many years ago by Mr. Robert Brown. We know that the particles are inorganic, and we are therefore quite sure that the movements we witness are due to physical forces alone.

Now, suppose we take a small fragment of dead animal or vegetable matter, place it in a few drops of water on a glass slide, and examine it with the microscope. The water appears as clear and transparent as the glass on which it rests. Next take both these slides and leave them under the same conditions for a few hours, taking care to allow the free access to them of light and air. At the end of three or four hours examine them again. First take the one containing the inorganic deposit of phosphate of lime, which for convenience we will call (A). You find that no change has taken place. There are the little particles still revolving as before in the fluid in which they are suspended. Some of them, indeed, may have become aggregated together, so as to form little masses, but beyond this there has been no change.

Examine the other slide, which we will call (B). You find that the fluid which, when you first looked at it, was perfectly clear, now contains a number of minute

granules closely resembling those of the phosphate of lime, and manifesting similar molecular movements. If you add a little gum, glycerine, or any viscid material to the particles on both these slides, you suspend the movements immediately, and if you dilute the fluid again, they recur. This indicates that in both cases the movements may be due to physical causes. The little particles which could move freely in such a limpid fluid as water, have had a check imposed upon them, as it were, by the tenacity of the substance we have added. Let both slides be again set aside for a few hours, and what shall we find on our next examination? In the slide A, containing the inorganic matter, no change has occurred; but the case is very different with B. The granules have increased considerably in number. Many of them have become altered, or their place is occupied by little bodies, some of which have a circular, others having an elongated form, but all exhibit a remarkably simple structure. If, again, a certain interval of time be permitted to elapse, and the slide B again examined, we find change still going on. The little bodies have become larger; in fact, they have grown, and have, moreover, increased considerably in number. It is easy to make out in the largest particles that the central portion differs from the exterior; in fact, that each is composed of at least two substances, or a substance in two different states. The changes I have described are characteristic of living particles. We know that the conditions under which B was placed were favourable to the development of certain simple living organisms. We have seen that at a certain period the granules on the two slides were scarcely

to be distinguished; but while those in A have remained unaltered, have retained the same granular form in which they were deposited, the particles in B have not remained stationary for a moment. They have grown, and have given rise to certain definite though apparently simple forms of matter, which still continue to manifest active changes. Here, then, you see an illustration of the fact which I mentioned to you at the beginning, that life is associated with constant change.

Now, the question arises, whence have these living organisms been derived? The water which we examined at first appeared perfectly transparent, and now it is filled with living structures. How did they come there? I have already told you that all living beings spring from preëxisting living beings. It has been stated, as you are perhaps aware, that simple organisms such as these may spring up spontaneously; but this statement is contradicted by facts open to the observation of all, and indeed it has been shown beyond all doubt that spontaneous generation, as it is called, never does take place. This doctrine of spontaneous generation has again quite recently been revived in France, and has of course been again refuted by an overwhelming mass of evidence. It has been shown that if the dead animal or vegetable matter be dried, and although so placed that the admission of atmospheric air which has passed through strong sulphuric acid is alone admitted, organisms will be produced, and all those phenomena, which we have already observed, will ensue. The ova which were protected in the interstices of the vegetable matter become developed into structures resembling those

from which they sprung. It is impossible to destroy the ova without destroying the vegetable matter which protects them. Thus the fact remains that living beings spring from preëxisting living beings. There is no such thing as spontaneous generation. These forms continue to exist and to grow so long as the conditions of life remain favourable, but when these are removed the organisms die. Now, if we examine one of these simple structures, we shall find that it is not the same in all its parts. It consists externally of a delicate membrane, and within of a material having a granular appearance. This is a point which it is most important you should remember, that in the simplest creatures two structures are to be observed, and that they possess very different properties. We shall see that this statement also holds good with regard to the elementary parts of the higher animals.

Structure of the simplest living organisms.—Suppose we examine a little ordinary mildew, which is one of the lowest forms of existence, and possesses a very simple structure. The little bodies which compose it are larger than those we have just been examining, and will therefore suit our purpose better. You will observe that it consists of a number of little round bodies. Each of these has a tolerably thick well-defined outline, while the interior presents numerous small particles like dots. Here, then, are two parts, the one situated externally, transparent, and arranged so as to form an investing membrane closed at all points, the other lying within, appearing granular, and presenting no form. Now, if you place these bodies under favourable conditions, certain changes will occur.

Let them be put, for instance, upon the moist surface of a glass slide, and after a time let the slide be placed under the microscope, and let us observe the changes which take place in the round spores. First of all, they absorb moisture and swell up, and the membrane appears to be thinner than before in proportion to the whole mass, and the granules seem to have increased in number.

Next, a new change is observed at one point in the membrane, a small orifice is formed, through which a little of the granular contents of the body covered with a thin layer of the inner part of the membrane passes, and thus a small nodule is formed which projects from the external surface of the membrane. By degrees this assumes a structure resembling that of the body from which it grows; it increases in size; the membrane around it becomes thicker; its point of attachment becomes less and less, until at last it is completely separated, and becomes a free and independent organism, exactly resembling that from which it sprung, and capable of giving rise to new individuals like itself, by a repetition of the process by which itself was formed.

This is one way in which the particles may multiply, but there are others. In this case, too, an orifice forms in the membrane of the particle of mildew, and a little of the granular material escapes, but it does not separate as in the first case; it remains in connexion with the mass, and grows out into a narrow thread-like process. The membrane on the external surface becomes thickened, and the whole increases in breadth. Within are contained a number of little spherical bodies or spores like those observed

within the circular body from which the process has grown. It may be that as this process grows at one or more points a thinning occurs in its wall, and a portion of its contents coming into more immediate contact with the pabulum increases in amount, and thus gives rise to the production of another process or processes growing from and exactly similar to the first.

Of the growth of simple living structures.—Now let us consider how this organism nourishes itself. The materials for its growth and nourishment are certain inanimate matters (solids and gases) existing dissolved in fluid in which the organism floats. These materials must pass into its structure and become part of it. That which is inanimate must become incorporated with and assume the properties of living matter. Now, if you place this structure under certain unfavourable conditions its vital properties will be destroyed. The granular matter in its interior will shrivel up and die, but this will be attended by no obvious alteration in the external membrane. The part which exhibits form remains, that which is without form is destroyed.

In the growth of the structures, then, how is the new matter produced? Does it take place by deposition upon the external surface of the investing membrane, or is the new matter produced by the granular matter in the interior? To put the question still more simply, Is the capsule, the so-called cell wall, formed by deposition of matter from the fluid surrounding it, or is it formed from within? and which is the oldest part of the capsule, its external or internal surface? If the new matter were

deposited upon the external surface, we should expect to find that the membrane would become thicker and thicker as the growth of the organism advanced, while the central portion would remain unaltered. This, however, is not the case; on the contrary, we find that as growth proceeds the wall in most cases becomes considerably thinned. It is clear, therefore, that the increase in size cannot be due to deposition from without. The matter deposited upon the inner surface of the capsule is always softer than its general substance, and the external surface of old capsules is always cracked and ragged. In many of the algæ this external surface serves as a nidus for the development and growth of smaller algæ—a fact which clearly shows it has ceased to be active and is incapable of resisting the action of external conditions. This is the oldest part of the capsule which is going into decay, and the small algæ are living in part upon the product thus produced. The new material is added upon the inner surface of the capsule layer after layer, and where there are several layers the innermost is the youngest, and the outermost the oldest portion of the structure. If this be so, it follows that the inanimate material for the nourishment of these structures must pass through the outer membrane, and be taken up by the granular matter within, which communicates to it the same properties and powers which this living matter itself possesses, and which it has inherited from preëxisting particles. At present we cannot get further than this. I am ignorant of the nature of the changes which occur, but I believe the facts as I have stated them to be true. The oldest parts of the organism are on the outside, the youngest

are within, and between these there must be particles of different ages in different stages of existence.

Now, when you examine the living granular matter within the capsule with the aid of very high magnifying powers (1700 diameters),* you see that the mass is composed of spherical particles, and if you examine the largest of these, you will find that it is composed of smaller spherules; and several facts which I have observed, justify me, I think, in concluding that all these spherical particles are composed of smaller spherules, and these of smaller ones, although, from the imperfection of our instruments, it is not within our power to put this conclusion to the test of direct observation. I believe that in the centre of these minute spherules are particles just becoming animate, particles that are just becoming endowed with vital properties. At a short distance from the centre are others that have existed for a little while; further still are particles yet older than these; and, finally, on the exterior of each little spherule are found the oldest particles of which the spherical particle is composed. Thus the most external portion, there can be no doubt, is formed by the gradual growth of particles which takes place from the centre to the circumference. The matter of which the membrane covering the whole mass is composed was once granular, and resembled that now in the interior, but the particles composing it have passed through various stages of existence. They now no longer possess those wonderful

* The one-twenty-sixth of an inch lately made for me by Messrs. Powell and Lealand.

properties which belonged to them at an early period of their life. They are incapable of growing, incapable of communicating vital properties to inanimate matter. The investing membrane or *cell wall* is *passive*, the granular matter within consisting of the so-called *cell contents*, and *nucleus* is the *active portion* of the structure. Such seem to be the changes that take place in the growth of the simplest living structure. Crude material is absorbed, and passes through the external membrane or envelope; it appears granular, but really consists of minute spherules: it passes through certain stages of existence, and at last a certain *form* is given to it. It may now become hard, or may be soft and soluble in fluid, and soon converted into certain peculiar compounds; but it ceases to possess those wonderful properties of communicating to inanimate matter its powers of growth and increase which belonged to it in the granular state.

Of germinal matter and formed material.—It is most difficult from mere observation to trace in a number of different structures derived from organisms occupying very different positions in the scale of created beings, the structures which exactly correspond; to show which structure represents, according to the terms generally employed, the *cell wall*, *cell contents*, *nucleus*, and *intercellular substance*. The discussion of this question has given rise to the greatest differences of opinion, and in many cases the subject has become so complex that it would require many lectures merely to state the case. I therefore propose to consider simply the matter in the tissues of the higher animals which corresponds to the substance *within*, and to

that of which the *external envelope* of the mildew is composed. Practically this is not possible by the ordinary processes of examination, but in an ammoniacal solution of carmine with glycerine, we have a fluid which will always tinge the internal granular matter of a structure for a short time after its death of a bright red colour, while it exerts no action whatever upon the external envelope or substance formed from this. It tinges the nucleus of a very dark red colour.

It would occupy too much time if I were to bring forward all the arguments I could in favour of the terms I have applied to matter in these two states, but I may mention a few of them. As the matter within is the active substance—as it exists in every tissue from the lowest organisms to the highest, in health and disease, and at every period of life—as it is directly descended from the germ, and is constantly producing germs, I propose to call it *Germinal matter*. As the outer structure is formed from this in all cases, although it differs very much in physical properties and chemical composition, I shall call it simply *Formed material*. *Germinal matter* removed from any organism which was recently alive, is tinged red with carmine, and retains this colour permanently when preserved in glycerine. *Formed material* is not coloured, but if it be stained, owing to the solution being too strong, the stain is removed by soaking in glycerine. I have specimens which have been preserved nearly three years which exhibit these characters as well as when they were first mounted. Every elementary part of every living organism may be considered to consist of matter in these

two different states. *Germinal matter* which, from inanimate nutrient material, will produce new germinal matter, and which becomes converted into *formed material*; and this latter substance, which was once in the state of germinal matter.

LECTURE II.

Of the tissues of the higher animals—Examination of cuticle—Tendon—Nerve fibre—Structure of germinal matter.

When we last met, Gentlemen, we were considering, you will remember, the manner in which the tissues of living beings are built up. I drew your attention to some of the principal theories which have been proposed, and pointed out to you that although these theories might serve well enough to explain the formation of some of the tissues, yet that there were others in the adult organism which it was almost impossible to conceive could have originated in simple cells, with wall, cell contents, and nucleus. It would be equally difficult, I think, to conceive the changes which occur, supposing them to exist at first as a simple homogeneous plasma, or as an aggregation of particles precipitated from a fluid. I then went on to say a few words on the characters of inorganic particles of matter, and asked you to view the changes which occurred in a drop of clear water containing a little dead animal or vegetable matter. We saw that granules appeared in the clear fluid, and that these granules resembled the inorganic particles in their general characters. Both specimens appeared to consist of simple granules; both exhibited molecular movements; and in both these movements were stopped by the addition of a viscid fluid;

but here all resemblance ceased between the two. The inorganic particles underwent no further change, while in the fluid containing the living particles, changes were continually occurring. The granules increased rapidly in number and in size, so that you could almost see them grow, and the fluid became darkened by their increased number. Not only did they grow and increase in number, but after a time they assumed definite forms, simple, indeed, but nevertheless definite forms, oval or circular. Each particle now consists of two parts; the one external, *transparent, and having the appearance of a membrane;* the other lying within this and consisting of a *soft material composed of a number of granules.* I then explained to you that these little living bodies formed no exception to the rule which I laid down in an early part of my lecture, *that all living beings spring from preëxisting living beings;* that they had been developed from minute germs which had found their way into the fluid from the air, or existed in the dead animal or vegetable matter. I alluded to the experiments performed both in this country and in France which prove this point beyond all question. I then asked you, as these particles were exceedingly small, to observe with me, under high powers of the microscope, the phenomena that occurred in other little particles, similar to, but larger, than the last, and therefore affording a better view of the manner in which they grew, were nourished, and multiplied themselves. The particles in question were the spores of ordinary mildew.

The chief points we made out from the investigation were these:—That the growth of these organisms does not de-

pend on the deposition of new material on their external surface; that the nutritive material, consisting of inanimate matter in the surrounding fluid, passed to their interior through the investing membrane, capsule, or cell wall; that it is in their interior that this crude material became endowed with vital properties; that as the particles grew new material became living in their centres, and the older matter passed towards the circumference. At the circumference it became converted into that substance which constitutes the cell wall or the capsule of the spore. I tried to show that this capsule was destitute of vital properties; it was unaffected by those conditions which would destroy the life of the granular matter within. It was once granular, active, and living, but the particles of which it was composed, in assuming a form, terminated the active period of their existence. The membrane thus produced takes no part in the vital changes which are going on in the individual; it serves merely as a protection to the delicate active structure within. I alluded to certain facts which prove that the granular matter is the active part of the structure, and whenever any of this escapes beyond the limits of the investing membrane, it gives rise to the formation of other bodies, exactly resembling in all essential characters the first.

Of the tissues of the higher animals.—We may now pass on to consider if these observations are applicable to the tissues of the higher animals. It may be stated generally that every living being, from the simplest creature to the highest and most complex of all organisms, is composed partly of granular material and partly of tissue, and I shall

endeavour to show that this tissue, like the envelope of the mildew, is formed from the granular material, and existed, in fact, at an earlier period in this state. The granular matter is always found within, the formed material on the outside of an elementary part. I propose to call this granular substance, as it exists in all living structures,

Germinal matter.—The term involves no theory, and it is a convenient one, for in any structure, at an early period of development, the germ consists of a granular material. It is the formative material, and we may conclude that from it all the tissues of the body are built up. That this is the material which is essentially concerned in those operations which we speak of as growth, nutrition, and development, and alone possesses the active powers of selecting pabulum, of growth, and of production of tissue, and of reproduction. The organism is made up of different tissues, and these tissues are composed of elementary parts. Each elementary part consists of *Germinal matter and Formed material* which was once in the state of germinal matter and was formed from it.

Now, germinal matter presents the same appearance, from whatever situation it may be obtained. Whether it be taken from nerve tissue, or from muscle, or from the simplest animal or vegetable organism, it possesses no distinguishing features by which its source may be determined. This cannot be said, however, of the properties it displays, for the rapidity with which it passes through its different stages of development varies considerably in different cases, and the products formed by it are very different. It may be shown that elementary structures consist of two parts—

germinal matter and matter formed from this or formed material. By a careful examination of tissues, both animal and vegetable, tissues in the young, in the adult, and in the old, in health and disease, and in those which constitute morbid growths, the truth of the above statements may be verified. It will be found that the proportion of the germinal matter to the formed material varies greatly in different tissues and at different ages, but in structures which grow quickly the proportion of germinal matter is always very great compared with that in slow-growing tissues.

Examination of cuticle.—Suppose we examine a portion of cuticle. The oldest portions (cells) of this structure are on the outside, and the youngest, or those which have been most recently formed, are situated nearest to the blood, from whence their nutritive supply is derived. If we make a section of this structure and place it under the microscope, we notice that different parts of it present different characters. That portion which is nearest to the vascular surface consists of small masses of germinal matter which are situated very close to each other. Examine a little above this and you find that the masses have a more definite arrangement, and each consists of an oval body which possesses an external membrane. Still nearer the surface the elementary particles appear more or less flattened, and consist of granular matter with a considerable quantity of cuticular substance or formed material (cell wall); and lastly at the surface, the elementary parts present hardly an indication of germinal matter (nucleus), and seem to be composed entirely of cuticular substance. Take equal portions of the most superficial and deepest strata, and the pro-

portion will be found to be considerably greater in the latter. Where the elementary parts are being produced the *germinal matter is abundant;* where they have grown old and finished their existence, the *germinal matter is reduced to a minimum, or has altogether disappeared.* Now, consider how these particles of cuticular epithelium grow. Here is a little mass of germinal matter, which grows and then divides into two, each of these subdivide, and so on. Now, each of these little bodies absorbs nutriment from the surrounding fluid. It increases in size. The older particles on its surfaee are altered and appear to be converted into a hard substance which is improperly described as a membrane (cell wall). As it approaches the surface of the body the hard material becomes thicker and thicker, forming the cuticular substance, until at length the germinal matter in the centre having nearly all undergone conversion into formed material, and being too far removed from the source of nutritive supply to increase at the same rate, the remainder perishes; by this time the elementary part in the form of a flattened scale of cuticle has reached the surface of the body, and is to be removed. Such is the history of the growth of cuticle.

Let us take some other structure—a portion of tendon of a fœtus.

Tendon is made up of the same firm, hard white substance of which you remember I told you fascia was composed: it is the tissue upon which the toughness and resisting property of skin depends, and the same tissue is met with in various other parts of the body where a structure with these physieal properties is required. Now, if

you examine a small portion of a tendon of a fœtus under a power of two hundred diameters, you find that it is composed of oval masses of germinal matter, with a certain proportion of intervening fibrous structure. At an early period of its existence it contained a much larger proportion of germinal matter. Now, the general form of the tendon has been laid down, and it has begun to assume the appearance of structure. If you watch its growth you will find that, as this proceeds, the fibrous material increases, and the germinal matter relatively decreases, so that when it reaches its adult form the principal portion of the structure consists of fibrous material, while there is comparatively only a very small quantity of germinal matter. To state this more clearly, I may say that in equal portions of fœtal and adult tendon the proportion of germinal matter is very different. There may be five or six times as much in the former as in the latter. The formed material increases as the tendon is developed, and at the same time undergoes condensation. The fibrous material has been formed from the germinal matter. It possesses no power of absorbing nutritive material and converting it into tissue like itself. All additions to its substance take place at those points only at which germinal matter exists. The little masses of germinal matter situated at regular distances throughout the tissue, and having the appearance of nuclei, are the only parts engaged in the process of growth,* and upon the outer part of each is a

* The anatomy of tendon and of various kinds of fibrous tissue was fully discussed in my lectures at the College of Physicians, which will be published shortly.

layer of soft matter in a transition state. It has ceased to be germinal matter and is about to become tendon. The inanimate nutritive material is absorbed by the germinal matter, and forms a part of the living matter. It goes through certain changes, and then, upon arriving at the circumference of each oval mass, is converted into the substance of which the tissue is composed.

Suppose we take another example. Let us examine nerve fibre and see how an elementary part of that tissue would be represented.

Nerve fibre.—Now it is in the terminal distribution of the nerve fibres that the structure of the elementary part is to be made out. The investigation is attended with great difficulty, in consequence of the extreme minuteness of the parts to be examined, and the great nicety required in preparing them for examination. The nerve fibres near their termination become diffluent within a few hours after death. Observers are not agreed as to the way in which the final distribution of nerve fibres to the tissues takes place. Some imagine that they end in points or in club-shaped extremities, and others believe that they terminate in loops. By some it is supposed that both these methods of termination may occur. In investigating this point some time ago I was fortunate enough to make some very successful preparations of muscular tissue which disclosed to me a method of distribution not previously observed.* I found that every elementary fibre of volun-

* Phil. Trans. for 1860, "On the Distribution of Nerve to Voluntary Muscle."

tary muscle received a vast number of nerve fibres which were spread out as it were so as to form a kind of net-work on its surface. These fibres contained numerous oval masses of germinal matter situated at short distances from each other along the course of the fibre. The distance of the masses of germinal matter from each other varies in proportion to the activity of the changes going on in the part. In an early stage of the growth of the fibre the masses of germinal matter are very close together, but as the growth of the fibre proceeds, the distance between the oval masses is increased. The germinal matter probably forms new tissue at either of its extremities, so that as the quantity of formed material is increased, the masses of germinal matter are farther and farther removed from each other. We see, then, that an elementary part of nerve fibre may be represented as an oval portion of germinal matter with an exceedingly delicate fibre projecting from either side of it.

I might go on to describe an elementary part of muscle, or of cartilage, or of any other tissue. In every case it would be found to consist partly of germinal matter, and partly of a substance formed from this, or *formed material.*

Structure of germinal matter.—Now, with regard to this germinal matter. It is, as I have said, the seat of growth, of nutrition, and multiplication, and it is met with in varying proportions in all living tissues.

You find it in greatest amount in young tissues, and as a tissue advances in development it diminishes. In many slowly growing structures, the proportion is very small. It is more abundant in actively growing structures; and this statement holds good in every case, at all ages, and in

morbid growths, as well as in healthy structures. In certain morbid growths, characterized by the rapidity with which they increase, the elementary parts are found to be almost entirely composed of germinal matter, with a very thin external investment. In those growths, on the contrary, in which the changes are less active, the elementary parts present an investing membrane of considerable thickness, and the amount of germinal matter in them is comparatively small.

I must now say a few words with regard to the structure of germinal matter. I have stated that it presents a granular appearance. It is difficult to say exactly what is the form of the ultimate particles. If, however, you examine a portion of germinal matter, you will find it to contain round particles of a determinate size; but among these are others so small that under the highest powers they appear as mere dots or granules. Among the particles there is generally one considerably larger than the rest. This is the body known as the *nucleus*. It is circular in outline, and is formed in the same way as the particles among which it lies. It is composed of granular matter, and often a particle larger than the rest can be discerned. and this is the *nucleolus*. The nucleus is a separate centre of growth, and if all the rest of the germinal matter outside this were destroyed the nucleus might retain its vitality. Now, I think from the general tendency which the particles of germinal matter have to assume the spherical form. as observed in the nuclei and in the germinal matter of mildew, and from the fact that some of the larger spherical particles are composed of smaller spherules, we may fairly

infer that the form of the *ultimate particles* of which these are composed is also spherical. Of course this is only an hypothesis. It is impossible to demonstrate such a point. Yet it seems an inference which one is justified in making from considering the facts which have been observed, and we may suppose that each of these particles is itself composed of smaller particles, and these of still smaller particles in different stages of growth.

The smallest particle is compound, and the particles of which it is composed are themselves compound also. For it is impossible to conceive a living particle of matter which is not compound. Impossible to conceive, for instance, a living particle of oxygen or hydrogen, or of iron, or of any simple substance, so that every living particle of matter, however small, must be looked upon as of complex composition. In this character it differs materially from an inorganic particle; and in the changes which are continually going on in these, changes which constitute the growth and development and multiplication of the particles, the most varied and complex chemical combinations are constantly occurring. These changes, however, although necessarily associated with the life of the particles, must not be looked upon as constituting their life.

Now, I believe that this germinal matter possesses unlimited powers of growth. So long as it continues under favourable circumstances it will continue to absorb nutritive material, and to convert it into living matter. The crude material being absorbed is converted into germinal matter, and as such has the power of animating new material, and changing it into a substance like itself, but after

passing through certain stages it assumes a form, it ceases to be granular, and then it no longer possesses the power of communicating its properties to inanimate matter.

Let us now consider why it is that the particles of germinal matter divide, and why it is that they never grow beyond a certain size? Throughout the whole of Nature this is found to be the case, and I do not know of a single instance of a single mass of germinal matter which can be found to exceed the 1-1000th of an inch in diameter. This is probably the utmost limit to which a living mass may attain without dividing into two, but in most cases the division takes place long before the masses have reached this size. Now, what would be the result if a mass of germinal matter went on growing until it attained a considerable size?

It is clear that the particles occupying the centre of this mass would be very far removed from the source of nutritive material. The pabulum for its nourishment would permeate the formed material which surrounds the mass; but before it had proceeded far on its way towards the centre it would be appropriated by the germinal matter lying nearer to the circumference, and so nourishment would never reach the centre at all. Thus, the central portion being entirely cut off from nutritive supplies, would become stationary. *That progressive movement of the particles from centre to circumference*, without which life cannot be, would be arrested. This central part would perish, and the products resulting would soon cause the death of the whole mass of living matter.

LECTURE III.

Recapitulation. The process of crystallization contrasted with the formation of living structures—The form of the particles of germinal matter—Changes occurring in elementary parts resulting from the conditions under which they grow being altered—The formation of tissues having peculiar properties depends upon the power of the germinal matter—Changes occurring when a blister is applied to the skin—The formation of pus—A certain bulk of young tissue contains a larger proportion of germinal matter than a corresponding bulk of old tissue—Of the white blood corpuscles and pus corpuscles—Of the process of secretion.

Recapitulation.—In my last lecture, Gentlemen, I ventured to suggest to you a theory with respect to the growth of living tissues different from those which have been hitherto proposed and generally received. I mentioned to you that all tissues, whether animal or vegetable, are made up of elementary parts, and that to these the term *cells* has been applied. Now, this term, as we have seen, is a bad one, inasmuch as the characters of the cell cannot be demonstrated in the elementary parts of many of the tissues of the higher and also of the lower animals and plants. I proposed to you, therefore, to give it up while pursuing this subject, and stated that we should simply consider what could be discovered of the process of growth by actual observation. We have seen that all elementary

parts are composed of two structures; the one having the characters upon which the peculiar properties of the tissue depend, the other possessing no structure, appearing granular, and presenting the same aspect in whatever tissue it may be examined. It has been seen that the substance on which the properties of the tissues depends is formed from the material with the granular appearance. To this latter I have given the name of *germinal matter*. This substance is found in greatest quantity in young tissues, and in the earliest period of their existence tissues are entirely composed of it. The germinal matter which is formed in the nerves or muscles of any of the higher animals cannot be distinguished from the germinal matter in the tissues of the leaf of a plant, or from that which exists in the particles of the lowest fungus. All tissues were once germinal matter, and the germinal matter gradually becomes converted into tissue. In certain cases in which the changes in the tissues are rapid, the germinal matter of to-day becomes the tissue of to-morrow. The pabulum of yesterday is germinal matter of to-day, and this is all that we can say. We know that inanimate material is absorbed into the living structure, and, under these circumstances only, becomes endowed with the properties of the particles among which it passes, but how the change takes place we cannot tell.

And this conversion of inanimate into animate material takes place, I believe, in the central portions of the elementary particles of germinal matter, so that the oldest particles are always on the outside, and the youngest always in the interior. Whatever be the form of the

mass, these remarks will hold good. I believe that in those cases in which a clear membrane, ordinarily termed the cell wall, exists, the substance of which it is composed was once germinal matter, and had the power of animating crude material, converting inanimate matter into living matter; but as soon as it became membrane, as soon as a form was given to it, or it exhibited structure, it lost these powers. The thickness of the so-called cell wall may be increased from within by the accumulation of formed material produced by the enclosed masses of germinal matter, or it may become thinner and much stretched, owing to the rapid increase of the germinal matter within, or the cell wall may be stretched and its thickness increased at the same time. In either case this envelope itself is passive.

The formed material which constitutes muscular tissue possesses the wonderful power of contraction, but it is quite incapable of converting crude material into tissue like itself; whereas the so-called nucleus of muscle, or as we call it, the germinal matter of muscle, while it is continually giving up its old particles to form muscular tissue, is always actively engaged in converting into material like itself the pabulum supplied to it from the blood, and in many cases it may be shown that the relative proportion of germinal matter to the whole mass diminishes as the growth of the tissue advances; or, in other words, as the formed material which is produced accumulates.

In the muscular fibres of the heart, and in some other forms of striped muscle, the germinal matter is in the very *centre* of the muscular fibre, so that each fibre is continually

growing from *centre to circumference.* The oldest part is outside—that is, on the surface of the fibre; while the new contractile substance is produced in the centre.

The process of crystallization contrasted with the growth of living structures.—Now, nothing like this occurs in the inorganic world. The formation of organic structures has been compared to crystallization. But if the account I have given of the growth of organisms and tissues be correct, it is clear that the two processes do not admit of comparison. For what takes place in the formation of crystals? A molecule of some substance held in solution in a fluid is deposited, other molecules of the same kind are deposited around this, and the particle goes on increasing, additions being made to its *external surface* until a mass perhaps of considerable magnitude results. But observe the portions which were first deposited; the oldest portions, as they may be called, are at the *centre of the mass*, the newest portions are on the outside, and all the particles from centre to circumference are motionless.

In living particles, on the other hand, we have seen that the old matter is at the circumference, and that all additions to the structure take place at the centre. The central particles possess active powers; they animate the new matter, and movement in a determinate direction, is constantly taking place.

Neither does the method of deposition of inorganic particles having a rounded form resemble the formation of living structures. In many round calculi, for example, the distinct strata of which upon section they are seen to be composed, clearly point out the method by which they have

been formed. The *nucleus of the spherical mass was formed first and the circumferential layers were last deposited.* One essential difference, then, between the formation of organic and inorganic particles is this, that in the case of the inorganic matter the mass increases by simple deposition of new material on its outer surface, while the organic particles grow by absorbing into their interior crude material, and converting it into living matter which undergoes changes and exhibits movements and certain phenomena which are not observed in dead or in inorganic matter, and which seem to obey laws different to those which govern inanimate matter.

The form of the particles of germinal matter.—Passing, then, from the region of demonstration, so to say, to that of hypothesis, we might consider what form the particles of germinal matter assume. It seems reasonable to suppose, as I have said, that they are spherical. But this is nothing more than a supposition, for it is impossible to see them: it is impossible to separate any portion of germinal matter into its elementary particles. We may, indeed, see particles that have a spherical form, but we know that these are composed of others smaller, and these again of still smaller particles which are themselves compound. For it is impossible to conceive a living particle of matter so small that it ceases to be compound. It is impossible to conceive a living atom. However minute it may be, if a particle of matter be living, it must consist of more than one simple elementary substance. But even supposing it were possible so to isolate the smallest spherical particles of germinal matter, and so to mag-

nify them by means of the microscope that their form could be demonstrated with some degree of certainty, yet it must be remembered that their condition would be very different from that which belonged to them in the living body. The properties of the matter would be so much altered by the manipulation required to prepare it for examination, that I doubt whether you could, from results so obtained, form any idea at all of the structure it possessed when it was living and growing in the body. For my own part, I believe that you might as well expect to resolve with the telescope the most distant nebulæ which that instrument reveals to the eye, or attempt to penetrate into the boundless regions of space, as think that you can bring into view by means of the microscope the ultimate particles of which living matter is composed. Increase the power of your instrument, and you do but see particles which were before invisible. You cannot hope by direct observation to ascertain how the component elements are related to each other in the living particles.

Changes occurring in elementary parts resulting from the conditions under which they grow being altered.—And now I propose to allude briefly to some of the principal changes which take place in the nutrition of the tissues of the body, and next to say a few words on some of the simplest changes which go on in disease. Why do we find the surface of the skin perfectly smooth and even—I mean, of course, the general surface? Why is it uniformly smooth and not irregular, growing thicker at some points, and remaining thin at others? This uniformity depends upon the maintenance, in all its parts, of an even balance

between two opposite processes, *of removal and repair*, which are always going on in tissues in a state of health. In every tissue new particles are continually being added, and old ones are being removed ; but the rate at which these changes go on is very different in different tissues and in the same tissue at different times. The proper activity of these processes constitutes the normal or healthy state of the tissue, and any influences which interrupt or suspend the due performance of these compensating changes produces an alteration in the structure, properties, and action of the elementary parts. I may illustrate these remarks by reference to one or two structures.

In cuticle in a state of health there is a constant addition of new particles taking place at its deep aspect, and these gradually pass towards the surface of the body, and increase in size as they pass outwards, in the same manner as the elementary structures which we have been examining. At the same time the old particles on the outer surface of the cuticle are being constantly removed. As fast as the old particles are removed from the surface, new particles are produced below, and so long as these two processes keep pace with each other the normal condition of the cuticle is maintained. But supposing the skin to be supplied with improper pabulum, or not supplied at all—supposing the blood to be contaminated with some noxious material which interferes with the due formation of new tissue,—in any of these cases the state of health is departed from, and a morbid condition is established. The old matter is removed from the surface, but nothing new may be produced beneath to supply its place.

A change of this sort occurs in scarlet fever. The morbid matter circulating in the blood interferes with the regular production of new cuticle; for a time none is formed, but by and by, when the violence of the disease abates, and the poison is in a great measure eliminated from the blood, the formative process is reëstablished. A gap, however, exists, as it were, between the tissue formed before the interference of the disease, and that produced after the natural process was resumed. In point of age they are separated by an interval, so that as the new cuticle grows up from below, the old is separated *en masse*. We may suppose that some change of this sort occurs in those creatures which, at regular periods, shed their skins as it is called.

The formation of tissues having peculiar properties depends upon the powers of the germinal matter.—With regard to the development of cuticle, we have seen that it takes place from masses of germinal matter resembling those which are found in connexion with all the tissues of the body. The tissues are all formed from germinal matter. From whatever tissue it be taken, it presents, as I have said before, the same general appearance, and it grows in the same way. But the results of its growth are very different in different localities. Thus in one situation germinal matter forms the matrix of tendon, cartilage, or bone, in another muscle, in another nerve, and so on. And although in all these structures it presents the same aspect, yet the germinal matter of muscle will not form nerve, nor will the germinal matter of nerve form muscle, nor can either of these tissues be produced from the germinal matter of

bone or cartilage. It is quite clear, therefore, that the germinal matter from each of the localities above mentioned possesses peculiar and distinctive endowments, although all these different kinds were originally produced from a single mass in the embryo.

If you transplant a little of the germinal matter of certain tissues into the substance of others it will produce, in its new situation, the material of the tissue from which it was taken. Transplant the germinal matter of bone and bone it will make.

The experiments of M. Ollier are of considerable value in proving this fact. He removed portions of the periosteum, the tissue you know which supplies the germs from which new bone is formed, and placed them in various situations among the superficial tissues of the body, and he found that wherever the bone-forming tissue was placed, it still produced bone. This is a very interesting fact, and it seems to me impossible to explain it upon physical grounds. It is not a mere precipitation or aggregation of preëxisting particles, or crystallization, or mere secretion; but it is an actual production or formation of a structure totally different in chemical composition and properties from the matter out of which it was formed—a process of formation very different to any phenomena occurring in the inorganic world. All that you can say of it is that it depends upon certain inherent properties in the germinal matter—properties which the living particles of which the germinal matter is composed can communicate to inanimate matter. The germinal matter of the different structures may be regarded as so many different kinds of germinal matter,

each possessing a peculiar inherent property: one to form bone, another to form nerve, another muscle, and so on through all the tissues, and each kind will, so long as it preserves its normal state, produce its own tissue, without reference to its position. There are certain morbid actions which serve well to illustrate this truth. Look, for instance, at what occurs sometimes in that disease which is known as bone-cancer. Certain minute particles, the germs of the growth, pass into the blood, and are carried by that fluid to different parts of the body. You can imagine how small they must be, since they pass through the finest lymphatic and capillary vessels of the system. The vital properties of these particles is so great, and their inherent powers of growth are so remarkable, that when their course is arrested in any part of the circulation, and they are deposited in any tissue, they take root, as it were, grow and give rise to the formation in that tissue of a structure resembling that from which they have been derived. In a case which came under my notice some time since, some of these germs of bone-cancer were deposited in the pulmonary tissue, and little masses of bony tissue were developed in the lung. I allude to these facts because they support the statements I have already made with regard to the inherent properties of unlimited growth which exist in germinal matter, and to show that its development into this or that tissue is not determined by physical causes, but depends upon some power resident in the germinal matter, which power it derived from preëxisting germinal matter.

Changes occurring when a blister is applied to the skin. The formation of pus.—Now, let us consider briefly the patholo-

gical changes which take place when a surface like that of the skin is irritated; as, for instance, when an ordinary blister is applied. The skin swells, fluid is poured out beneath the surface of the cuticle, so as to separate this structure into two layers. By the accumulation of the fluid the superficial layer of the cuticle is pushed up, and thus a *blister* is raised. I say the *upper layer*, for it is not the whole of the cuticle that is thus raised up, but only the oldest portion. Now, if you examine the deep surface of this layer as soon as the blister is raised you find that it consists of a number of elementary parts, each having a thick outer wall, with a central portion of germinal matter which is very distinct. In the subjacent fluid, too, if you look you will find a number of such particles floating about separately. If the irritation be kept up for some time longer you would obtain at last a viscid fluid holding in suspension a vast number of bodies composed almost entirely of germinal matter, and having a very thin investing membrane of formed material. They are growing and multiplying rapidly. The *débris* of the tissue and the nutrient matter determined to the spot seem to be absorbed by these particles, and converted into living germinal matter. These bodies are pus corpuscles. The effect of the irritation is such that the elementary parts of the cuticle are produced with greater rapidity than in the normal state. Nutritive material is supplied from the blood, and supplied in greater abundance than usual, and this must be converted into living material. If it were not so converted the whole of the surrounding tissues would perish. For if the nutritive plasma did not become organized, it would

undergo decomposition, and we know that the substances produced by such a change would infallibly destroy the vitality of the tissues amongst which they were produced. The nutritive material, then, is converted into germinal matter in the ordinary manner, but so rapidly do the subsequent changes occur that there is no time for the gradual production of cuticle. The elementary parts of cuticle are formed by a process of slow and gradual transformation of germinal matter as it grows old, into cuticular substance; but in the morbid state produced by the irritation of the blister, this gradual transformation cannot take place, and elementary parts consisting almost entirely of germinal matter, with very little formed material, are alone produced. Flakes of a very soft spongy structure resembling cuticle are first formed, and these give place to the development of the substance we know as *pus*. In the process of healing the order of the change is reversed. The formation and multiplication of germinal matter gradually diminishes, and time is allowed for the proper cuticular material to be formed. This is a simple explanation of the changes which occur when a blister is applied to the surface of the skin as far as I have been able to observe them.

I think now we have been over some of the chief points with regard to the formation of tissues from germinal matter. The embryo consists almost entirely of germinal matter, the separate masses of which divide and subdivide, until the basis of each tissue is laid down. Then the oldest particles of the germinal matter of each mass becomes converted into the particular substance of which the tissue is to consist.

A certain bulk of young tissue contains a larger proportion of germinal matter than a corresponding bulk of old tissue.—In all tissues the quantity of germinal matter diminishes as age advances. The relative proportion of germinal matter to the formed material in certain tissues is less in the adult condition than in youth, and less in old age than in the adult state. This may be illustrated by examining the muscles of insects in the larvæ at different stages of growth, and again in the perfect state. In the young larva you find in a given amount of the tissue a much larger proportion of germinal matter than at a later period, and in the perfectly formed tissue the quantity is reduced to a comparatively small amount. The same is true of man. In the embryo, germinal matter abounds, and the development of tissues takes place rapidly. In the adult, development still goes on, but to a more limited extent; and so with regard to the reproduction of lost parts. In early life the reproduction of tissue is effected rapidly and with wonderful facility; but as age advances we find this power diminishing, until in old age even union of some tissues will not take place at all. The production of new material for the repair of injuries in the old is a difficult process, and on examining their tissues we find that the proportion of germinal matter to the formed material is small, and this active matter is often imbedded in a very thick layer of formed material which prevents the free passage of nutrient matter to it.

Of the white blood corpuscles and pus corpuscles.—We have spoken so far of the germinal matter as it occurs in the solid tissues of the body. But it is not confined to these.

It is to be found also in the fluids of the body. Thus, the white corpuscles of the blood, the corpuscles of the lymph and chyle, and the contents of the closed glands are to be regarded as masses of germinal matter possessing important powers of growth. The white corpuscles of the blood increase in number in certain cases of disease with great rapidity. They do not undergo the natural change into red corpuscles at the same rate at which they are produced, and so the balance which I spoke of as existing in health, between the opposite processes of production, of new matter and removal of old, is destroyed.

From what I have already said with regard to the circumstances which determine the proportions of germinal matter to the formed material in an elementary part, you will see at once why there should be so great a resemblance existing between chyle and lymph corpuscles, certain corpuscles in some specimens of mucus, the corpuscles in certain glandular organs, white blood corpuscles, and pus globules. All these bodies are composed almost entirely of germinal matter, the masses of which grow and are free to move in viscid fluid. Many of them could not be distinguished from spherical masses of germinal matter existing in the lower animals. They are all coloured by carmine, and exhibit the same general characters. I need scarcely remind you that their powers are very different; and here we have one of the many instances which might be adduced to prove that no idea of the powers of germinal matter can be formed from its general appearance, or from any tests we are yet able to employ.

The white blood corpuscles are simply masses of germinal

fluid, and the constant motion to which they are subjected by the circulation of that fluid prevents their undergoing any process of development into tissue. But let them become stationary from any cause, and they give rise to the formation of a simple kind of fibrous tissue—indeed, there is reason for believing that fibrin is the *formed material of the white blood corpuscles.*

In cases where the lymphatic glands are enlarged and the quantity of fibrous tissue considerably increased, I believe that the fibres in the substance of the gland are formed from the lymph corpuscles. In the spleen I have seen tail-like processes projecting from the white corpuscles, and it is easy to find corpuscles in every transition from the spherical colourless corpuscle to the nucleus with fibrous tissue projecting from different parts of its surface and continuous with it. These fibres in fact seem to be formed from it.

Of the process of secretion.—And now, before I conclude this lecture, let me draw your attention for a few moments to the consideration of the process of secretion. Let us examine it in the liver. Here is a representation of a liver cell. In the diagrams of these structures which you meet with generally, you find a well-defined round or oval body containing a nucleus, delineated. But in reality, when you come to examine the structures for yourself, you find no such regularly-formed body, and some of the cells have a very irregular outline which is often angular and sometimes ragged, so as to give you the idea that it is being disintegrated. It contains within several smaller oil globules.

Now, one cannot demonstrate the constant existence of

any membrane or cell wall around this so-called liver cell. The cell wall is *not a necessary* part of the cell. We will not speak of it as a cell, then, but rather as a mass of *formed material and germinal matter.* The germinal matter (nucleus) contains separate centres of growth, smaller masses of germinal matter (nucleoli) growing and appropriating to themselves new material, and capable of becoming a structure like the whole mass, so that all might be destroyed except the nuclei and nucleoli, and these retaining their vitality would commence to grow anew. Now, in the secretion of bile, this, I believe, is simply what takes place. The material from which the bile is to be formed transudes from the bloodvessels, it is absorbed into the interior of the mass constituting the "liver cell." Here it is converted into the material of which the germinal matter is composed. The particles of this mass are constantly growing from centre to circumference, and when they have reached the circumference of the mass, having passed through various stages of their existence, they become bile. So that in secretion the same rule is observed that we noticed in the growth of tissues. The conversion of new material begins at the centre, germinal matter is the form which it first assumes, and the particles of this substance towards the end of their life give rise to particular tissues, or, in the process of secretion, to the peculiar substance which is resolved into the constituents of the secretion.

In conclusion, let me say, without employing any technical terms, that the numerous facts I have referred to seem to show that every living being, and the particles of

which the active portion of every living elementary part is composed, consist of,—1. *Matter which possesses the power of forming itself into, or of altering the arrangement and relation of its own constituent elements so as to form, matter having certain peculiar properties*,—2. *Matter or tissue which has thus resulted or has been formed.* The latter generally forms an investment around and protects the former; but in certain cases, besides this investment being formed, some of the living particles undergo change, and become resolved into a peculiar *formed* matter which gradually accumulates to such an extent that the *forming* matter, of which very little remains, is found between the external investment and the *peculiar formed matter* within. As examples of this, you may remember I adduced the familiar instances of the fat-cell and the starch-cell. In nutrition, the pabulum first becomes *forming matter*, and in this new state passes through certain stages of existence, and at last becomes *formed.* The movement of the particles always takes place in *one constant direction*, *from the centre*, at which they became living. The pabulum always passes in the opposite direction.

LECTURE IV.

Granules or molecules—Dr. Bennett's molecular theory of organization—Globules—Cells or elementary parts—Nuclei and nucleoli—Fibres—Membranes.

Gentlemen,—Having considered some points with reference to the anatomy, modes of development, and growth of elementary parts, and having discussed the character of the changes occurring during nutrition, and the modifications which take place in these phenomena when the normal conditions are altered, we may now study the anatomy of the elementary tissues. Let me, however, in the first place, direct your attention to some of the bodies which are seen in certain textures and fluids of the organism.

In the examination of the tissues we meet with matter in the form of *granules* or *molecules*, *globules*, *fibres*, *perfectly clear transparent and apparently structureless membranes;* as well as matter forming definite masses, which possess vital endowments, and are therefore characteristic of living beings, and exhibit a peculiar structure. These are known as *nucleoli*, *nuclei*, and *cells* or *elementary parts.*

Granules or molecules.—I would define a granule or molecule to be a particle which is too small to exhibit any form or structure when examined by the highest magnifying powers we possess. It appears as a very minute point

or dot. We cannot say that these particles do not possess any definite form or structure, but at the present time no optical instruments are sufficiently perfect to enable us to arrive at any conclusions on these important questions.

With reference to the question of composition. Granules may be simple or compound, composed of one substance or many substances. They may consist of inorganic matter, or they may be composed of organic matter. They may be living or dead.

Each living granule possesses inherent powers of growth and multiplication. It may grow and divide, and the resulting particles may become developed into structures having very definite characters and possessing remarkable powers.

The inanimate granules, on the other hand, may coalesce to form larger masses, instead of dividing to form a greater number of particles, they may become crystalline and undergo other changes; but, it need scarcely be said, they are destitute of all powers of growth, properly so-called, and of reproduction.

It is of the utmost importance to draw a distinction between living molecules or granules and inanimate matter in this state of extremely minute division. As far as I am aware, it would be impossible, from the *general microscopical appearances alone, to distinguish the living from the lifeless molecules.* Neither do the movements of the particles help us to draw any distinctions, for in both cases movements are observed, and the motion seems to be of the same character. This is *molecular motion*, which is quite independent of vitality, and is seen to occur always when

minute particles of any matter are suspended in a limpid fluid. I have considered the general points observed in the examination of living and lifeless particles at some length in the Archives of Medicine, vol. ii., p. 185. It is only by watching the particles for some time that we can positively distinguish between these granules or molecules which differ in so marked a degree from each other in power. The inanimate particles, if they alter at all, undergo changes which can be accounted for by their chemical or physical properties. The living particles under favourable conditions, *grow*—not by the aggregation of several to form a larger mass or collection, as occurs in the case of the lifeless particles,—but each individual increases in size. It absorbs the matter which surrounds it, and causes a complete alteration in the properties of this matter. So far from the living particles collecting together and forming aggregations, they increase in size and divide and subdivide. They separate from each other, instead of collecting together, and this not by reason of any repulsion existing between the particles, but in obedience to a power resident in the living matter which compels the particles to move in a direction *from* the centre where the matter of which they are composed became living.

The inanimate granular or molecular matter present in certain animal fluids, or in the tissues, may be due to *insoluble albuminous matter*, *fatty matter*, or *saline matter*, in a state of very minute division.

The granular appearance depending upon albuminous matter in a state of minute division, is removed by the action of acetic acid or an alkali; that due to the presence

of fatty matter by ether; and that depending upon saline matter by water, acids, or alkalies, according to the nature of the substance.

Dr. Bennett's molecular theory of organization.—I have endeavoured to draw a distinction between the *inanimate granules* or *molecules* which may be *precipitated* from fluids, and the *living molecules* which *spring from preëxisting molecules.* For although, as a general rule, very small particles do not exist separate from each other in a living state, I have adduced reasons for believing that living independent organisms exist which are so small as not to be visible by the highest power until they have lived for some time and grown.*

Dr. Bennett considers that living structures are composed of *histolytic* and *histogenetic molecules*, or *molecules of disintegration* and *molecules of formation.* "The histogenetic molecules are formed either from the union of two simple organic fluids, or from precipitations occurring in formative fluids holding various substances in solution." "The histolytic molecules are the result of the transformation and disintegration of fluid and solid substances by chemical

* Dr. Bennett applies the term "granule" to a body with a light centre and a darkly shadowed outline. A small spherical particle of oil exhibiting these characters would therefore be spoken of as a "granule," while a larger one would be termed a "globule." I have thought it better to restrict the terms "*molecule*" and "*granule*" to particles of matter which exhibit no structure, and are too small to show a clear centre with dark outline, and that of "*globule*" to bodies in which a dark outline and transparent centre can be distinguished.

and mechanical action." Under the head of histogenetic molecules, Dr. Bennett describes the molecular matter produced by an admixture of oil and albumen, and shows how the latter may be caused to coagulate in the form of a membrane on the surface.

He considers that the molecules are formed by a physical process, and that afterwards they become aggregated together, so as to form masses around which the cell wall is formed. According to these views, then, the living cell, endowed with the power of forming peculiar substances, and of producing other living structures like itself, is produced in much the same way as the artificial cell consisting of oil and albumen with an insoluble envelope, which possesses none of the powers characteristic of living cells.

The living cell is formed by the *aggregation* of living particles, the artificial cell by the *aggregation* of lifeless particles. In each case the membrane is supposed to be thrown around the collection, and the "cell" is complete.

Now, a living "molecule" placed in a fluid containing inanimate matter will grow, and will gradually assume the appearance of a collection of molecules, but the growth does not depend on the *aggregation* of a number of molecules. The substances passing into the interior are in solution, and the molecular appearance results from subsequent changes. Again, a number of minute living particles being suspended in fluid never run together and form collections. So far from aggregating together, *they divide and subdivide, and multiply enormously in number.* Inanimate particles always become aggregated together, or coalesce to form larger masses. Living particles never

become aggregated to form a compound living mass, but each absorbs nutrient matter and divides into smaller masses. The living particles multiply in number, radiating from, instead of collecting towards, centres.

Before inanimate substances can become living they must be reduced to the state of solution, and there is reason to believe that at the moment when the matter becomes endowed with vital properties the relation of its component elements to each other becomes totally altered. These elements being afterwards arranged in obedience to powers resident in the living matter, in such a manner as to give rise to the production of certain definite compounds, and as these compounds are formed, the material ceases to exhibit those endowments to which, it seems to me, the term *vital* should be restricted.

It has been shown that the outermost part of the so-called "cell wall" is the oldest portion of the structure, and that it is increased in thickness from within. Hence, according to Dr. Bennett's view, we must suppose that two distinct processes take part in the formation of this structure. Matter from the surrounding medium being first deposited over the surface of the mass, while this is afterwards thickened, not by the addition of new layers upon the external surface, but by matter which is deposited from within.

It seems very unlikely that the outer layers should be formed in a totally different manner to the layers within, for very often it resembles these so closely that no line of demarcation exists, and no difference whatever can be demonstrated.

Sometimes masses of living matter exhibit a stellate appearance, and are completely destitute of any "cell wall" whatever. Portions may be seen to project from the general mass for some distance, as if growing from it into the surrounding medium. These processes often break off, and thus from one individual mass, many separate masses may be formed. Each one of the resulting portions grows and gives origin to new masses by division.

In fresh mucus, the manner in which the living masses, which appear to be composed of molecules, multiply, can be seen very readily. Portions project from the general mass, become detached, grow, and divide. These masses are always coloured by carmine, and can thus be distinguished with certainty from the collections of inanimate oil globules and molecules which are seen here and there, and resemble them in general appearance.

No demonstration of the precipitation of living particles from a clear fluid has yet been made by any one; while, on the other hand, it is easy to adduce examples in which the origin of an aggregation of living molecules from a pre-ëxisting living mass can be traced most conclusively. The process can be seen quite distinctly in every stage in various epithelial structures, and in the lower plants and animals it may be actually observed to take place under the eye of the observer.

I have endeavoured to show that every elementary living structure is composed of matter in two states, and that a difference exists in the manner in which these two portions behave towards certain colouring matters. The differences observed in appearance, in chemical charac-

ters, and physical properties, between the matter of which the "cell wall" and the "cell contents," in many cases, is composed, are due to the different stages of existence of the different parts at the time of examination. One part consists of matter which is just beginning its life; the other of matter which has already passed through the various phases of its existence. The matter which is endowed with the most active powers is darkly coloured, while the matter which has ceased to possess the power of multiplication and selection is not coloured at all. By the action of carmine and some other colouring matters the so-called "cells" formed in the living body can be at once distinguished from structures resembling them in form which are prepared artificially. Moreover, when the living particles have been removed for some time from the body they cease to exhibit these characters. They are, in fact, dead. These and other points which I have referred to before, seem to me to militate against Professor Bennett's view of the formation of living molecules by precipitation from organic fluids. Very many facts are in favour of the doctrine, that living molecules spring only from preëxisting living molecules, and that the formation of living cells or elementary parts takes place in a manner *totally different to that in which bodies resembling them may be formed artificially.* The former possess inherent active powers, by virtue of which the matter composing the living particles is caused to acquire new properties, and its elements are separated and then made to unite to form new combinations. Particles possessing these powers can communicate them to new particles. The

artificial bodies have no such endowment, but any changes occurring in them can be explained by well-known physical laws.

Globules.—A globule may be defined to be a body which appears under the microscope to be circular, with a dark outline and transparent centre. Globules are generally spherical, but they may be oval or irregular in form. They differ much in size. The smallest body, which appears as a distinct globule when examined by high powers, of course might be termed a granule or molecule, if subjected to examination, only by low magnifying powers. In composition, globules vary as much as granules. A little milk placed under a power of 200 diameters affords a good idea of the characters of globules. In this case the globules are composed of fatty matter, but it is often quite impossible to distinguish oil-globules from globules of phosphate of lime or some other saline matters, without resorting to chemical tests. Frequent mistakes of this kind have been made.

You must bear in mind that the thickness of the outline of a globule depends upon the difference between the refractive power of the matter of the globule itself and that of the medium in which it is immersed. The same globule of phosphate or carbonate of lime will appear almost entirely black, when examined in air, to have a very thick dark outline when placed in water; while in oil or turpentine, or Canada balsam, or even in syrup or glycerine, the outline will appear as a thin dark line. In estimating the character of a globule you must bear in mind the influence of the medium in which it is immersed upon its appearance.

The term globule is only properly applied to bodies having the above characters which are composed throughout of one substance. A particle of mildew might be termed a globule, and this might be brought forward as an example of a series of facts, the knowledge of which has led some observers to believe that there exists a great resemblance in structure and microscopical characters between inanimate and living particles. Examined in air or water it might be impossible to distinguish the inanimate globules of phosphate or carbonate of lime from the living spores of mildew, but the greatest difference between them is demonstrable if proper methods of examination be employed.

The inanimate globule is often of the same constitution in all parts. If acted upon by chemical solvents it dissolves slowly from the outer surface towards the interior, and the part which was first deposited (the centre) is the last to disappear. The spore of mildew, on the other hand, is composed of matter having very different properties—externally of a thick firm membrane, within which is soft matter in an active living state. The membrane or envelope may be ruptured, and its contents caused to escape. If placed in carmine the membrane is not coloured, while the soft matter within is coloured red. If placed under favourable circumstances the soft matter within grows. In all these and many other important characters, the spore of mildew differs from a globule of phosphate or carbonate of lime, and it would therefore be quite unreasonable to say that an inanimate globule is formed in a manner at all resembling that in which a living structure like the spore of mildew is produced.

The matter of the inorganic globule is merely *deposited* from its solution in fluid. The living structure which appears like the inanimate globule, when examined in a superficial manner, has the power of forming the materials of which it is composed out of matter which is totally different from the compounds produced. Not only does chemical combination take place, but the elements, by the powers of the structure, are caused to assume a certain arrangement, the result of which is the formation of the chemical compounds characteristic of that particular living structure.

Cells or elementary parts.—I have already described what is generally understood by the term *cell*, and have endeavoured to show that the definition usually employed cannot be applied to the elementary parts of many tissues. We may, however, use this term, which is very short and convenient, if we give to it a more general meaning. I would venture define the cell or elementary part as a structure always consisting of matter in two states, *forming* and *formed*, or *germinal matter* and *formed material.* The first or active substance is surrounded and protected by the outer passive matter, through which all the pabulum to be converted into germinal matter must pass.

An aggregation of oil-globules or calcareous particles caused to cohere by intervening viscid matter, or invested by a similar substance, will appear very like a form of cell. Such bodies exist in the organism and have been described as cells, but similar appearances can be produced artificially. Such bodies do not take part in the *formation* of compounds. They may undergo chemical and physical changes, but it

need hardly be said they have no power of growth or multiplication. No nucleus or anything corresponding to it can be demonstrated upon the application of carmine. This action of carmine on the living growing matter has not been generally recognized, and inanimate structures which do not possess any inherent powers of *forming* or *producing* have not been distinguished from structures which possess these wonderful properties in a marked degree. There is often a great similarity in general appearance, but there is a total difference in power. The aggregations of particles under consideration may be *stained* by carmine and other colouring matters, but the colour is uniform and is easily removed, and they never exhibit those different tints which are so striking in the true cells or elementary parts, and which can only be explained on the view that different parts of the living structure exhibit different properties or possess different degrees of activity.*

Nuclei and nucleoli.—True nuclei are always coloured by carmine more deeply than the matter which surrounds them or in which they seem to be embedded, and nucleoli are more darkly coloured than the nuclei. Nuclei and nucleoli are new centres which are developed in preëxisting *living matter*. In many cases mere oil-globules have been mistaken for nucleoli. The manner in which nuclei and nucleoli make their appearance in germinal matter has

* The varying intensity of the action of carmine on the different parts of the vegetable cell is illustrated in the drawings of the Rev. Lord S. G. Osborne.—"Vegetable cell structure and its formation as seen in the growth of the wheat plant."—Transactions of the Microscopical Society, Oct. 1856.

already been described, and these living structures can always be distinguished by their becoming darkly coloured, while oil-globules do not receive the colour at all. Although we cannot in many cases distinguish living granular matter from inanimate granular matter by mere observation, we can always do so most positively if we resort to the process of staining with an ammoniacal solution of carmine, or some other alkaline colouring matter.

Fibres.—Anything which appears as a mere line, or solid and thread-like, with a double outline, may be termed a fibre. Some fibres are so fine as scarcely to be demonstrable, others so thick as to exhibit a boundary-line on each side and a considerable thickness of matter between. When a fibre is thick in the centre and gradually tapers off into thin lines at the two extremities, it is called a "fibre-cell," although the meaning of the word fibre is utterly opposed to that generally given to the word "cell," which is held to be a closed vesicle with certain contents in its interior. The definitions given to words in general use in this department of knowledge are often very vague and unsatisfactory, and in many cases the meaning becomes in the course of a very few years greatly modified, although the term is still retained. Any tissue exhibiting lines parallel to each other, and exhibiting regularity, or arranged irregularly, crossing and interlacing in various directions, is said to exhibit a "fibrous appearance," which may be due to the mode of formation of the tissue (tendon, periosteum, &c.). Such an appearance may be produced artificially in some perfectly clear substances by the addition of chemical reagents.

Membranes.—Transparent and apparently structureless membranes are met with in various tissues in the human body. The outer portion of the elementary part exhibits these characters in many instances (cell wall). In this case the clear membrane is formed by condensation taking place in the formed material, while at the same time it may become increased in extent by stretching, produced by the growth of the germinal matter, or by the accumulation of secondary deposits, within. In some instances a clear transparent membrane seems to result from changes occurring in preëxisting structures. Capillary vessels and delicate nerve fibres, with a small quantity of intervening tissue, may form a thin layer, so smooth and clear as to resemble a membrane. There are instances in which numerous elementary parts united together at their edges form a membranous structure. As such a tissue grows old, all distinction into cells is lost, and the whole appears as a transparent membrane.

An appearance resembling a transparent membrane may also be produced artificially by the application of certain chemical reagents to various structures, and sometimes by the action of acetic acid or potash, a homogeneous layer is produced on the surface of a tissue, which is very likely to mislead the observer, and lead him to infer that a true membranous investment exists, while in reality there is no trace of such a structure.

LECTURE V.

THE TISSUES.

On the classification of tissues—Of the connective tissue theory — Cells and intercellular substance — Canalicular System—The connective tissues—Tendon—All fibres which resist the action of acetic acid, not elastic tissue—The fibres of yellow elastic tissue are not tubular—Cord-like connective tissue—Cornea—Sketch of the changes occurring during the development of tendon and allied tissues.

I SHALL not attempt to divide the tissues into certain specific classes, because it appears to me that it is not possible at present to suggest a classification which would be of any real assistance to the student.

The following classification is, with slight modifications, generally accepted by writers on the subject:—1. Cell tissues. 2. Connective tissues. 3. Contractile tissues. 4. Nervous tissue, or the last two are included with the vessels in a group by themselves, and termed the "higher tissues."

Classifications have been made according to the physical properties of tissues, and according to the offices which they serve. There are objections to all these plans. In many cases a tissue would fall into a different class at different periods of its development and growth.

In my first lecture I discussed at some length the anatomy of cells or elementary parts as they occur in the so-called *cellular tissues*, and I propose now to de-

scribe the anatomy and properties of the most simple fibrous tissues of the body. Many of these are connected with the locomotive organs. Afterwards I shall pass to the consideration of the more elaborate structures. In the first place, I must give a general description of the tissue, then we shall be able to consider the mode of its development, and to study the changes occurring during its growth and decay. Lastly, I shall briefly refer to some of the general modifications occurring in its growth, and alterations produced in its structure which are observed in disease.

On the connective tissue theory.—It is not too much to say that the so-called "connective tissue series" forms one of the most important groups into which the tissues of animals have been divided. Certain examples of this class of tissues exist from a very early period of development, and some representative of the series may be demonstrated in all except the lowest classes of animals and plants. In man and the higher animals, some of the connective tissues perform most important and special offices, and some are found in every part of the body. Soft connective tissue is said to form a connective medium between other tissues, a supporting tissue to higher structures. It extends with the vessels into every organ. It is in contact with epithelial structures, and in some cases is continuous with them. It is connected with nerves and vessels, and exists between the elementary fibres of muscle. It is found in the most delicate nervous structures, as the retina, brain, and cord, and exists in considerable quantity in connexion with the peripheral distribution of nerves.

Firm connective tissue exists in the form of white fibrous tissue in ligaments and tendons, in periosteum and perichondrium, and in a granular, fibrous, or more or less homogeneous form in different varieties of cartilage and fibro-cartilage. Hard connective tissue is seen forming bone and dentine. The vitreous humour of the eye is said to resemble the so-called mucous tissue which lies between the vessels of the umbilical cord, and these are adduced as examples of a very simple form of soft connective tissue. Contrasting with these structures, which are so very soft and contain in their interstices such a large amount of fluid, we have the hard and comparatively dry osseous and dentinal tissues.

You will, no doubt, have felt some surprise that this class of connective tissues should have comprised structures of the most different physical properties and chemical composition—tissues which grow very quickly, and tissues which increase so slowly that their growth is only perceptible at long intervals of time—tissues which, like bone, are undergoing with wonderful regularity constant change throughout life, and structures like the dentine of the permanent teeth, which remains almost without change, which is in part worn away by friction, the remains being ultimately altogether detached from the body—tissues which are entirely composed of "cells," like some varieties of cartilage, or like other forms, contain cells with a certain proportion of intervening matrix, and structures which are destitute of cells, like some forms of fibrous tissue—tissues which, closely surrounding capillary vessels, receive an abundant supply of nutrient matter, as well as tissues

which are separated a considerable distance from vessels, and receive but a small quantity. You will see at once that I have some reason for objecting to a classification of such a character as this, which seems to me to fail in fulfilling the main objects which we hope to attain by arranging facts in separate groups or collections.

Cells and intercellular substance.—In spite of such different properties, offices, and composition, these tissues undoubtedly possess certain characters in common, but it seems to me that these common characters have been very much exaggerated. It has been truly said that many are very closely related to each other, and that some pass one into the other, that in certain cases one may take the place of the other, and all may pass into bone. It must, however, be observed that epithelium and nerves and vessels and muscular fibre which cannot be included in this series, are continuous with connective tissue. It has been said that all these tissues consist of *cells* and an *intercellular substance*, and many hold that the latter substance is formed independently of the former; but I shall endeavour to show that such a distinction does not exist in nature, and that the so-called "intercellular substance" corresponds to the "wall" of an "epithelial cell."

Canalicular system.—Virchow has advanced a step further in defining the character and raising the importance of the so-called connective tissues. He states that in many of the soft connective tissues where the cells have a reticular arrangement, anastomoses take place just as occur between the canaliculi of bone or the branches of the dentinal tubes, and he professes to have demonstrated such tubes in

different forms of ordinary connective tissue, as tendon, mucous tissue, &c. "These anastomoses constitute a peculiar system of tubes or canals which must be classed with the great canalicular systems of the body, and which, particularly forming as they do a supplement to the blood and lymphatic vessels, must be regarded as a new acquisition to our knowledge, as in some sort filling up the vacancy left by the old vasa serosa which do not exist. This reticular arrangement is possible in cartilage, connective tissue, bone, and mucous tissue, in the most different parts; but in all cases those tissues which possess anastomoses of this description may be distinguished from those whose elements are isolated, by the greater energy with which they are capable of conducting different morbid processes."

As, however, there exist forms of connective tissue in which no *tubes* can be demonstrated but which contain *fibres of yellow elastic tissue*, some observers have gone so far as to consider this yellow elastic tissue as representing the nutrient tubes, and have not hesitated to assert that, because in some cases a cavity can be demonstrated in the yellow elastic tissue, there can be no doubt that this forms part of a "canalicular system" for conveying nutrient juices. Thus, various appearances have been interpreted in such a manner as to accord with the views of the structure and functions of connective tissue which have been propounded; but I shall show you that a number of points far more striking, and facts easy of demonstration which cannot be explained by the favourite theory, or which militate against it, have not been noticed in

the same prominent manner, or have been altogether passed over.

In every branch of natural knowledge facts are so numerous, that if we permit ourselves to be so misled it is easy to select a number in favour of many proposed theories, and thus the most conflicting doctrines sometimes seem to be supported by positive facts. All the connective tissues have, in fact, been brought into the same category as bone which consists of "cells with communicating tubes," and "an intercellular substance."

I have considered this question at some length elsewhere,* and I shall not now attempt to repeat the facts and arguments advanced in favour of my conclusions. I propose to describe briefly the general anatomy of those tissues which are of especial interest to us in connexion with pathological changes, in the following order:—White fibrous tissue, mucous tissue of the umbilical cord and the vitreous humour of the eye, yellow elastic tissue, cartilage, bone, dentine, muscular fibre, nerves and vessels.

Tendons, ligaments, and fasciæ, owe their firmness and unyielding properties to the white fibrous tissue of which they are composed. This white fibrous tissue is very widely distributed, but it differs materially in character in different parts. The three structures above mentioned are all composed of white fibrous tissue having well-marked characters. Parcels or collections of finer fibres varying somewhat in diameter are bound together

* "On the Structure of the Simple Tissues of the Human Body." Churchill. 1861.

with areolar tissue to constitute the tendon, ligament, or fascia. The few vessels and nerves distributed to tendon pass amongst these bundles, which in ligaments and tendons run parallel to each other, so that in a transverse section you see the different parcels packed together with the vessels between them. In fascia the bundles cross each other at different angles and form flattened bands.

Perichondrium and periosteum are also composed of white fibrous tissue; but these differ in structure from the white fibrous tissue just described, in several important particulars.

White fibrous tissue enters into the formation of the *areolar tissue* which is found between the various elementary organs, which make up an entire organ, and it forms a bond of union between the different textures of the body. This structure has of late years received the name of connective tissue. It contains yellow elastic tissue, but the proportion and characters of this latter tissue differ very materially in different kinds of connective tissue. Both these tissues, white fibrous and yellow elastic tissue, exhibit marked differences of structure in different parts of the organism, and I shall be able to show you that white fibrous tissue is formed in different ways, and that its properties and offices are very different. Some forms are developed from nuclei, like other tissues; while in other cases the fibrous tissue seems to be but the remains of more important tissues. Certain forms are present in the embryo, while others which exist in considerable proportion in the adult are not to be detected at an early age. The same remarks also apply to the yellow elastic tissue.

It must, however, be borne in mind that the microscopical appearances usually considered to be characteristic of these tissues may be produced without either being present.

It will, therefore, be necessary for me to depart somewhat from the plan generally followed in describing the anatomy of these tissues. I shall try to describe what may be actually observed if the tissue under consideration be submitted to microscopical examination. After the minute anatomy of some of these forms of connective tissue has been carefully considered, we shall be in a position to discuss the connective-tissue question generally. I may, however, as well again remind you that all the connective tissues are considered to consist of "*cells*" and an "*intercellular substance.*" It is generally held that the latter is produced independently of the former, and although Kölliker, like Schwann, has always most positively, and I think most correctly, maintained that the white fibrous element of connective tissue of tendon, for instance, is not formed independently of cellular bodies,—many of the highest authorities hold an opposite view, and regard this tissue as produced altogether independently of cells.

TENDON.

This structure is generally subjected to examination after having been dried, or partially dried, and then re-moistened with fluid, but it has been found that these processes cannot be carried out without some considerable alteration in the characters of the tissue being produced. The specimens referred to have therefore been

prepared without any desiccation at all. They have been soaked in carmine solution, and afterwards mounted in glycerine, according to the method already given. If a thin longitudinal section of tendon be examined, numerous narrow elongated bodies connected together by narrower lines, and arranged parallel to each other, and nearly equidistant, will be observed throughout the fibrous substance of the tendon. These are the "nucleated fibres of the tendon," or the parallel nucleated fibres, the *kern-fasern* of the German writers. The parallel, wavy, and delicately fibrillated matter between them is the white fibrous tissue of the tendon, the so-called *matrix* or *intercellular substance*, which is considered to be formed independently of, and not to be connected with, the nuclei. The proportion which the "nuclear fibres" bear to the quantity of the fibrous substance is different at different periods of development. If you examine the tendon of a fœtus, that from a young individual, and from an adult of the same species, you will find that the "nuclear fibres" are nearer together in the fœtus than in the young animal, and closer together in the latter than in the adult. In other words, as the tendon grows the fibrous tissue or intercellular substance increases in proportion to the nuclear fibres; or in a given bulk of tendon, the nuclear fibres are much more numerous in the embryo than in the adult.

If the tendon be stretched longitudinally, the nuclei become narrower and appear as mere lines. On the other hand, if the structure be stretched laterally, the nuclei are made to assume an oval form, and the extension may be carried so far as to cause them to be wider from

side to side than from end to end. The germinal matter thus extended forms but an exceedingly thin layer. The circumference is not so darkly coloured as the central part. Passing in a longitudinal direction are a number of lines (or rather the particles of which the germinal matter is composed, exhibit a linear arrangement) which run parallel with the fibres of the tendon, and these lines in the germinal matter may be seen, if a very high power be used, to be continued into the tendon, as imperfectly formed fibrous tissue. The direction of the fibres of the tendon is indicated by the arrangement of the particles of the germinal matter. These points which bear in an important degree upon the nature of the so-called "nuclear fibres" can be demonstrated very distinctly in specimens of tendon which have been prepared in the manner I have described, and afterwards subjected to stretching and pressure. The appearances are represented in Fig. 34, Plate VI. of my lectures "On the Structure and Growth of the Tissues," delivered at the College of Physicians in 1861.

The appearances I have described will lead you to the inference that the nuclei are continuous in all cases with the fibrous tissue of the tendon. The fibrous tissue (intercellular substance) nearest to the nuclei or masses of germinal matter, is that which was most recently formed; while that which is most distant is the oldest portion of the tendinous structure. Continuous with the particles of germinal matter is imperfectly formed fibrous tissue. As the germinal matter is exceedingly soft and undergoes changes soon after death, and is destroyed by the action of water, it is not surprising that the continuity of structure

between the germinal matter and the firm fibrous tissue should not have been generally reeognized ; but if eare be takeu to eolour and harden the germinal matter, this eontinuity is made out very readily in every kind of fibrous tissue.

If tendon thus prepared be earefully torn up with needles, very delicate bundles may be separated ; and it is not uncommon to find the oval masses of germinal matter with portions of white fibrous tissue projecting from either extremity.

From the faets that these oval bodies are eoloured by earmine like the nuclei of other tissues, and the fibrous tissue of the tendon is in direet continuity with them, we eannot but conclude they are the masses of *germinal matter of the tendon, and bear the same relation to the fibrous tissue that the germinal matter bears to the formed material of other tissues. This is the living matter which takes part in the formation of the tendon.* As this view is quite opposed to the notions generally entertaiued, it will be neeessary for me to diseuss the auatomy of this tissue more at length.

If a pieee of adult teudon be treated with aeetie acid, the parallel nuelear fibres beeome more distinet in consequence of the fully developed fibrous tissue being rendered elear and transparent by the action of the acid. Arouud the bundles of fibrous tissue are, however, other delieate fibres which resist the aetion of aeetie acid. These appear like fibres of elastie tissue.

First, as to the delieate fibres of yellow elastie tissue which encircle the fibrous bundles of many speeimens of tendon.—

It has been assumed, I think much too hastily, that these elastic fibres are in connexion with the nuclear fibres. Their existence is undoubted, but they are not in sufficient number to be considered as essential constituents of the tissue, and they are not to be detected in all forms of white fibrous tissue. For the most part they wind round the bundles. By great patience you may occasionally succeed in finding a nucleus connected with some of these fibres, but when this is so, the nucleus is very small, and quite distinct from those I have described as connected with the white fibrous tissue. It is, however, so seldom that I have been able to demonstrate this nucleus in connexion with the yellow elastic tissue in tendon, that as I have seen this appearance result from alterations produced in an undoubted capillary vessel, I am disposed to explain the very few cases in which I have met with it in this manner. At an early period of development the tendon is, comparatively speaking, very freely supplied with blood, and it is possible that some of the elastic fibres which encircle the bundles may be the remains of nerve fibres and capillary vessels.

As a rule the fibres *encircling* the bundles of the white fibrous tissue are certainly not connected with nuclei. The nuclei which are constantly present, exhibit a linear arrangement at every period of the growth of tendon, and they are in its substance. The yellow elastic tissue, on the other hand, is not arranged in parallel lines, but the delicate fibres of which it is composed form a lax network on the surface of the bundles.

The masses of germinal matter which I have described in tendon and allied tissues are regarded by Virchow as

areolar or connective tissue corpuscles, "bindegewebs-körperchen," and he states that they are connected together by tubes, so as to produce a stellate arrangement. In a longitudinal section he admits that nothing of the kind is to be seen, but in a transverse section the stellate arrangement is observable. It seems to me that this may be explained thus:—It is not possible to obtain a very thin section in which all the divided parts are *in situ.* In the transverse sections made, some of the prolongations from these bodies are altered in position, so as to make it appear as if they passed amongst the longitudinal fibres and established a communication between the different nuclei.

If you attempt to make a transverse section, the stellate bodies are undoubtedly seen, but it is impossible to obtain a very *thin transverse section* of tendon with these nuclei in their natural position. In trying to do so, you cut off short pieces of tendon and the included nuclei, with their prolongations of germinal matter and imperfectly developed formed material which resists the action of acetic acid, being altered in relative position by the pressure to which the specimen is subjected, appear like stellate cells or corpuscles with radiating processes. In all cases, however, in properly prepared specimens, the continuity of structure between the nuclei or masses of germinal matter, imperfectly developed formed material, and fully formed fibrous tissue, can be demonstrated.

In some specimens of young tendon these prolongations from the masses of germinal matter *(cells* or *nuclei)* are well seen, and their communications are tolerably numerous. The processes are distinct enough in some places,

but most of them gradually become lost among the wavy fibres with which all are connected, and of which they are but the early stage. Although they somewhat resemble fibres of yellow elastic tissue in their general appearance and in their power of resisting the action of acetic acid, they are not of this nature; their outline is irregular, and when examined with very high powers they have a granular appearance, which is very different to the sharp outline and homogeneous appearance of the yellow elastic tissue.

Moreover, it must, too, be borne in mind that the appearance so remarkably distinct in certain specimens in my possession is not constant. It is not seen in a specimen of adult tendon where fibres of yellow elastic tissue are found, nor in that of a kitten; and in the fascia of the frog there is no more indication of such an arrangement than there is in cartilage. In some specimens of the tendon of the child which have been stretched and pressed, the appearance of stellate cells and communicating tubes is most distinct, but that it depends upon an alteration produced in the nuclei, and upon the displacement and tearing of some of the young tissue connected with them is sufficiently proved,—by the appearance being produced by pressure, by its absence in parts of the specimen not subjected to pressure, by the great variation in the appearances when the arrangement is produced, and by its entire absence in certain specimens.

The dark lines extending between the nuclei are not composed of elastic tissue at all, but consist of germinal matter and imperfectly formed tendon. The structure is

merely an early stage of fibrous tissue. The oval nuclei and intervening lines may be regarded as spaces and tubes in tendon some time after death, but in living tendon, and in tendon shortly after its removal from the dead body, the oval nuclei are composed of *living germinal matter* which extends from one to the other in the form of a very narrow line. Soon after death this germinal matter becomes broken down, and *there remain oval spaces and narrow tubes containing fluid and the products of its disintegration.* In the case of fibrous structures like tendon, where the fibres are parallel to each other, which are increasing in length and breadth as development advances, we should expect that the nuclei would multiply by transverse and longitudinal division, but as the fibrous tissue is continuous throughout the length of the tendon, the oval nuclei remain connected together end to end, while the division laterally is more complete. At the same time, in some cases, when the nuclei are dividing laterally, they retain connexion with each other. These connexions become finer and finer as the formation of fibrous tissue continues, and in certain specimens appear as narrow lines passing between contiguous nuclei.

The fibres of yellow elastic tissue are not tubular.—Not only has it been inferred that the nuclear fibres are composed of yellow elastic tissue, but it has been stated that yellow elastic fibres are hollow and convey nutrient juices to the tissues through which they ramify. Virchow very cautiously expresses himself on this point as follows:—"It has not up to the present time positively been determined, whether in the course of this transformation, the

condensation of the walls of the cells proceeds to such a pitch as entirely to obliterate their cavity, and thus completely destroy their powers of conduction, *or whether a* small cavity remains in their interior. *In transverse sections of fine elastic fibres it looks as if the latter were the case*, and there is therefore ground for *the supposition*, that in the transformation of the corpuscles of connective tissue into elastic fibres, nothing more than a *condensation* and *thickening*, and at the same time a chemical metamorphosis of the membrane takes place, but that ultimately, however, a *very small portion of the cell-cavity remains*."

In yellow fibrous tissue, from many situations, I have seen prolongations of germinal matter as in other tissues, but I have completely failed to prove that these yellow elastic fibres generally are tubular, and concerned in the distribution of nutrient matter. Over and over again, I have stained the nuclei amongst the fibres of yellow elastic tissue with carmine, while not a single fibre exhibited the slightest alteration. I cannot think, therefore, that these fibres at any period of their development really consist of tubes for the transmission of nutrient juices. The very fine transverse lines which are seen connecting the oval nuclei of some specimens of tendon precisely correspond, as I have already stated, to the prolongations by which they are connected together in the longitudinal direction, and in nature there are to be found examples of every shade of structure, disconnected masses of germinal matter, masses connected longitudinally, masses connected laterally and longitudinally at right angles, in a stellate, or in a most irregular manner.

All fibres which resist the action of acetic acid not elastic tissue.—The imperfectly formed fibrous tissue (nuclear fibres) resists the action of acetic acid, while the fully formed fibrous tissue is rendered transparent by it. This power of resisting the action of acetic acid, like true elastic tissue, has caused observers to conclude that the nuclear fibres are of this nature; but it must be borne in mind that nuclei generally resist the action of acetic acid, and we use this reagent so much in anatomical investigation because it possesses the property of rendering the fully formed tissue transparent, and thus the nucleus or *germinal matter*, and recently formed matter around it, become much more distinct.

It has been assumed that all fibres which resist the action of acetic acid are composed of *yellow elastic tissue*, while the fibrous tissue which is rendered transparent and loses its fibrous appearance when subjected to the action of the same reagent is regarded as *white fibrous tissue*, or the *intercellular substance* or matrix of connective tissue. So also it has been concluded on what seems to me very insufficient grounds, that this intercellular substance is produced in the same manner, possesses the same physical and chemical characters, and performs the same offices in whatever organism or in whatever part of an organism it may be found. I think I shall be able to convince you that these conclusions are premature, and I believe that a too ready assent to this doctrine has not only prevented us from learning the truth with regard to the nature of many tissues, but has led us to entertain very arbitrary, and, I think, somewhat incorrect views with reference to the

nature of the process of nutrition in health. It has also encouraged erroneous views as to the nature of various pathological changes.

The consideration of this question involves the anatomy and history of the changes occurring during the life of most of the tissues of the body, and it must, therefore, be postponed until we have carefully traced the changes occurring in these tissues at different periods of age, but I think I shall be able to demonstrate that nerve-fibres and the corpuscles or nuclei which are constantly found, and in great number, in connexion with their terminal ramifications, capillaries and their nuclei, as well as some other structures, have been included under the indefinite term *connective tissue.* This phrase seems to me to have been employed by anatomists under very much the same circumstances as the term *extractive matter* has been used in animal chemistry. Any texture in which well known anatomical elements have not been demonstrated has at once been classed as *connective tissue.* We shall see that by employing different processes of preparation very definite and highly important structures are rendered evident, and we shall prove that the tissue possesses far higher endowments than are generally attributed to any form of connective tissue.

I must now briefly refer to some peculiar forms of this so-called connective tissue, in which certain fibres which resist the action of acetic acid are very distinct.

Cord-like connective tissue.—There are certain cord-like fibres in connexion with different organs of the frog in which we are able to study the mode of production of cer-

tain appearances which are observed in connexion with certain forms of fibrous tissue of the higher animals. The peculiarity I refer to consists in this, that fibres of a structure resembling elastic tissue seem to be embedded in a mass of white fibrous tissue. Many of these elastic fibres are connected together, and here and there nuclei are found. Often two branches seem to diverge from a nucleus, and the fibres vary much in diameter.

In several specimens of these cord-like fibres connected with the arteries, from the abdominal cavity of the frog, the following points may be observed :—

A bundle of nerve fibres is perhaps seen running in the external coat of an artery. Some of the fibres are seen to leave the large trunk of the nerve and run in the central part of one of the fibrous cords, which are continuous with the areolar coat of the artery. A portion of one of these cords with most distinct nerve fibres may be seen in one part of a specimen, and in another, a transition may be traced from most undoubted nerve fibres to the very narrow branching fibres before described. These fibres are not altered by acetic acid, and by careful examination it is clearly proved that they may be split up into finer fibres if they are not actually composed of several minute fibres collected together; so that they are not composed of the determinate fibres of yellow elastic tissue. Some of the finest of these cord-like fibres of connective tissue seem to consist of a transparent matrix in which two or three nerve fibres are embedded. The transparent tissue might be considered as the so-called tubular membrane of the nerve fibre. It seems to me, therefore, that the nuclei and

delicate fibres continuous with them, embedded in a more or less fibrous connective tissue, are nerve fibres which, if not functionally active, have been so at an earlier period of life, and that the matrix in which they are embedded corresponds to the so-called tubular membrane.

There are other cord-like fibres in connexion with some of the tissues of the frog which are a little like those just described, but are formed in a very different manner, and are destitute of the peculiar fibres which resist the action of acetic acid above alluded to. The mode of development of these thick cord-like fibres of connective tissue may be clearly traced in the cutis of the frog. Numerous oval nuclei may be seen undergoing division which occurs transversely and longitudinally. The distance between each gradually becomes increased, and for some time granular matter may be seen intervening between one nucleus and the other. In this case a reticulated arrangement exists, as in certain forms of fibrous tissue; and the fully formed tissue forms a variety of connective tissue between tendon and fascia, where the nuclei form straight lines: and the outer part of the periosteum and areolar tissue generally, where they assume a stellate form.

It is difficult to distinguish the points to which I have adverted in every individual case, but that fibres resembling elastic tissue in their behaviour with acetic acid, are immediately continuous with nerves, and remain in situations where nerves had been abundantly distributed at an earlier period of life will, I think, be fully proved in a future lecture.

CORNEA.

The transparent proper tissue of the cornea is a modification of white fibrous tissue. It is composed of a number of branching fibrous fasciculi which are closely adapted to each other. These fasciculi are for the most part arranged in laminæ which run parallel to the surfaces of the cornea. The fasciculi of one lamina are, however, continuous with those of adjacent laminæ. The arrangement of the bundles of fibrous tissue is such that a net-work is formed, the fibres of which are so closely adapted to each other that in the healthy cornea, intervening spaces can hardly be said to exist. Between these bundles, or amongst the fibrous tissue composing them, are situated the so-called radiating *connective tissue corpuscles*, or nucleated cells of the cornea. These were discovered by Mr. Toynbee in 1841. They are believed to be peculiar to undeveloped elastic tissue, and are considered to be connected with channels for conveying the nutrient juices. Even Kölliker, who nevertheless maintains that white fibrous tissue is developed from cells, considers these cells or nuclei to be distinct from the fibrous tissue, and accepts Virchow's explanation of their office. He remarks: "It is probably beyond doubt, that the nutrient fluid, which continually saturates the cornea in large quantity, is chiefly conducted and distributed further into the interior by the cells in question." If this be so, the nutrient fluids are circulating in channels which lie between the fibrous bundles that are to be nourished. On this supposition it is not easy to explain by what process the fluid is made to

pass into the interior of the bundles, and by what forces constant change in the particles of fluid is effected.

I have already occupied much time in demonstrating the anatomy of tendon, and I must not now trouble you further than to state as my opinion, what you will already have concluded to be so, that these so-called radiating cells and fibres are the masses of germinal matter of the cornea, are continuous with the fibrous tissue, and are directly concerned in its formation. These nuclei are much more numerous in a given bulk of young, than of fully developed tissue. *The fluids attracted towards these nuclei pass through the substance of the fibrous bundles*, and thus the integrity of the tissue is preserved. They have, I believe, nothing in common with yellow elastic tissue, except that, like this tissue, they resist the action of acetic acid.

Sketch of the changes occurring during the development of tendon and allied tissues.—Regarding the oval nuclei as the masses of germinal matter, and the fibrous structure which is in all cases connected with these, as the formed material, it is not difficult to account for the actual appearances observed in the different forms of fibrous tissue. At an early period of development these tissues like all others are composed almost entirely of germinal matter. The small masses of germinal matter increase, divide and subdivide in the soft imperfectly developed formed material which exists between them at this early period. In some tissues the masses of germinal matter soon become quite detached and entirely separated from each other, in which case, the tissue will consist of formed material with the separate masses of germinal matter embedded in it. In others the

masses of germinal matter divide in one particular direction, and partial or perhaps complete separation of the resulting masses occurs laterally, while longitudinally they still remain connected together; in which case, as the tissue advances in age, and the masses of germinal matter become separated from each other by gradually increasing distances, we should find the formed material arranged in parallel layers between the oval masses of germinal matter which would be connected together end to end by distinct lines of germinal matter and imperfectly developed formed material, and laterally, by finer and less obvious lines produced in the same manner. In other cases where the expansion of the tissue takes place equally in all directions, or equally in length and breadth, and the masses of germinal matter do not become detached, the tissue will consist of a matrix in which stellate masses of germinal matter are embedded. The radiating processes gradually becoming finer and finer as the tissue advances in age, until at last they quite disappear or leave a narrow line of imperfectly formed tissue which differs in chemical characters from that external to it, and resists the action of acetic acid like yellow elastic tissue. In tissues which are fundamentally composed of white fibrous tissue the most different appearances may result owing to the directions in which the structure is to expand, the rapidity of its growth, and the influence of stretching or pressure. In the structure of various forms of fibrous tissue in the human organism, wide differences are observed, but in some of the corresponding tissues of the lower animals the differences are so great that if only their anatomical characters were studied one would

scarcely believe that they possessed any general relationship. For instance, contrast tendon with periosteum, and either of these tissues with the imperfectly developed fibrous tissue of the umbilical cord or placenta.

On the other hand, there are examples of fibrous tissue which resemble each other very much in general characters, but which totally differ in their mode of formation and in essential particulars. Compare the cord-like fibres of the cutis of the frog with the fibres which have a very similar shape, and possess the same general appearance, in connexion with the larger vessels. The first consist of true fibrous tissue with its nuclei or masses of germinal matter. The last contain nerve fibres and often capillary vessels, and the "fibrous tissue" itself appears to result from changes taking place in these structures. Again, I have a specimen of thick false membrane which was taken from the surface of the liver, which, in parts, so closely resembles the proper tissue of the cornea, that without great care you might easily mistake it for this more highly developed form of fibrous tissue.

Before we decide upon the nature of many tissues, it is therefore necessary to trace their mode of development and growth, and anatomical relations, as well as to study their physical properties and chemical characters.

LECTURE VI.

FIBROUS TISSUES.

Connective Tissues.—Mucous tissue of the umbilical cord—Vitreous humour of the eye—Yellow elastic tissue—Formation—Kölliker's new view—Objections—The author's observations—Certain fibres of elastic tissue not formed directly from nuclei — Of certain changes occurring in fibrous textures in disease—Fatty degeneration—Death of the tissue—Effects of an increased supply of nutrient matter—Suppuration.

Closely allied to the so-called ordinary connective tissues are those tissues which have lately been grouped together by Virchow under the head of *mucous tissues.* The most important of these are the mucous tissue of the umbilical cord and the vitreous humour of the eye. The mucous tissues are characterized by their soft consistence and, as the name implies, by their general resemblance to ordinary mucus.

MUCOUS TISSUE OF THE UMBILICAL CORD.

The arteries and vein of the umbilical cord are connected together by a quantity of soft tissue which seems to correspond to the connective tissue external to an artery, and serves to connect the arteries with the vein to form the cord. This is one of the forms of connective tissue in which Virchow maintains the existence of special nutrient channels which anastomose with each other, and thus form a

system of communicating tubes for the conveyance of nutrient materials to every part of this tissue, which is destitute of capillary vessels. Virchow states that in a good preparation "a symmetrical network of cells is brought into view, which splits up the mass into such regular divisious that by means of the anastomoses which subsist between these cells throughout the whole of the umbilical cord, a uniform distribution of the nutritive juices throughout the whole of its substance is in this instance also rendered possible." I have completely failed in my efforts to discover anything like the arrangement Prof. Virchow has described. This "mucous tissue" consists merely of a soft form of connective tissue, in which the fibres correspond exactly to the fibrous tissue (intercellular substance, as it is generally termed) of ordinary tendon. The interspaces between the finest of the fibres seem to be occupied with soft transparent granular matter.

The fibres with the numerous nuclei are for the most part arranged to form the boundaries of more or less circular spaces. In the spaces are seen more delicate fibres arranged without much regularity, and the nuclei are much less numerous in the central part of the space than they are amongst the fibres which bound it. As the tissue grows the formation of new fibres takes place at the circumference. The nuclei of the older fibres die, and a great part of the fibrous matter itself is gradually softened and disintegrated; so that the circular spaces are gradually increasing in diameter as the tissue advances in age.

An elementary part of this tissue consists of an oval mass

of germinal matter, with ragged fibres projecting from either extremity, and often extending for some distance. Many of the elementary parts are triangular, and the fibres pass off in three directions. The fibres have the general appearance of fibres of ordinary connective tissue, and the germinal matter extends for some distance in opposite directions, gradually tapering into a very thin line, which is at length lost amongst the fibrous tissue. In the fresh tissue, therefore, there are no communicating tubes and lacunæ, as Virchow has described. The drawings which I have made of my specimens do not at all resemble the diagrams he has given of the same tissue. Compare figs. 41, 42, pp. 98 and 600, of Dr. Chance's "Translation," with figs. 37, 38, plate vi., of "The Structure of the Simple Tissues." What appears to be a space or cavity in the centre of the elementary parts is really occupied with germinal matter, and the apparent tubes contain prolongations from this imperfectly-formed and soft fibrous tissue. This soft germinal matter breaks down very soon after death, and thus spaces and tubes may result. These tubes do not exist as channels in the tissue during life, and the nutrient matter permeates every part of the tissue instead of flowing through any special channels.

Although it has been stated that the muscular fibre cells of the artery exhibit a totally different structure to these elementary parts of the mucous tissue, by reference to the drawings, you will observe there is some considerable resemblance, and that the relation and mode of formation of the formed material in both structures are the same, although the properties of the formed material are very

different in these cases. I have gone somewhat into detail with reference to the minute anatomy of this structure, because Virchow regards this as one of the tissues the structure of which specially favours his view, and there is a most important question involved in this inquiry. The conclusions we form will influence our views upon the nature of the process of nutrition generally.

VITREOUS HUMOUR OF THE EYE.

There still exist among observers the greatest differences of opinion regarding the anatomy of this clear transparent tissue which contains more than 99 per cent. of water. Many years ago Mr. Bowman showed that in the infant at birth the vitreous was represented by a structure very much resembling the so-called enamel organ, and composed of elongated cells, with processes apparently of a fibrous character radiating from them. Virchow regards the vitreous as an example of "mucous tissue," and considers that in the fully-developed vitreous humour the cells have disappeared, leaving only intercellular substance with mucus which he has detected in this structure. Kölliker agrees that at an early period the vitreous is composed of embryonic connective tissue. He considers "that subsequently, at least in its inner parts, every trace of this structure disappears, so that it comes to consist of a more or less consistent mucus.

The adult vitreous appears to be homogeneous, and not even the remains of cell structures or any indication of fibres can be detected in its substance. It is true

that some observers have stated that even in the adult, cell structures were to be found in certain parts, and quite recently E. Neumann of Königsberg, has stated that he had convinced himself positively of the existence of cells in the vitreous of adult animals and man. I have carefully examined this structure in several different ways, but have little to add to the observations of Bowman and others. It seems to me that the vitreous closely resembles the transparent tissue which surrounds the ova of the frog and other batrachia. This latter tissue after having been dried swells up again to a considerable extent when placed in water, though not to its original bulk. Cellular elements are to be seen in this at an early period of its formation; but when fully formed it seems to be composed of a very delicate tissue, probably the finest fibrous tissue that can well be conceived. It contains less than one per cent. of solid matter.

Upon the inner surface of the hyaloid membrane, which is continuous with the vitreous, round masses of germinal matter exist, which are separated from each other by pretty regular intervals, and from them a very soft tissue can be traced into the vitreous, with which it is, in fact, continuous. In freshly effused lymph the fibres are combined with so large a quantity of fluid as to be invisible, but gradually as the matter of which the fibres consist becomes condensed, the fluid is expressed by their elasticity, and they gradually become sufficiently thick to be seen as definite lines under the microscope. If it were not for the elasticity of these fibres and their tendency to condense, we should not be able to form any more positive

opinion as to the structure of lymph than we can of the vitreous. I look upon the vitreous as a form of very delicate fibrous tissue, the fibres of which are combined with a very large quantity of water, and consider that it bears to the so-called cells above referred to the relation of formed material to germinal matter in other situations. I should conceive that the oldest part of the vitreous was that towards the centre, while the circumferential portions were last formed, and it is probable that this structure during life undergoes very slow change indeed. The hyaloid membrane may, perhaps, be a highly condensed form of a tissue resembling that of which the vitreous itself is composed.

YELLOW ELASTIC TISSUE.

Yellow elastic tissue differs from the white fibrous tissue in anatomical characters and in physical and chemical properties. Of a yellowish colour, very flexible, generally composed of cylindrical fibres varying much in diameter in different localities, it is eminently elastic, and it retains its elastic power after removal from the body. This tissue may be preserved for many years in preservative fluids without its important physical property of elasticity being in any way impaired. The elastic power of this tissue is often antagonized by muscles, and the delicate movements of the ponderous head of the ruminant are due to the contraction of the flexor muscles of the neck, by which the elevating action of the elastic ligamentum nuchæ is antagonized.

In the following situations true yellow elastic tissue is

found with well-marked characters: *Ligamentum nuchæ: ligamenta subflava: chordæ vocales:* many ligaments about the larynx; in the *stylo-hyoid ligament* and *suspensory ligament* of the *penis*, and a modified form is found in the *elastic coat of arteries*, in the *trachea* and *bronchial tubes* and *pulmonary tissue.* Fibres of elastic tissue occur in connexion with the *subcutaneous*, *submucous*, and *subserous* areolar tissue; and fibres generally considered to be of the same nature exist in connexion with tendon and almost all forms of white fibrous tissue. The true elastic tissue is always connected with, and developed from, nuclei, but there are many fibres, ordinarily considered as yellow elastic fibres, which are but the remains of tissues (nerves and vessels) which were active at an earlier period of life.

Although elasticity is the property which is universally characteristic of yellow elastic tissue, this structure does not exhibit an anatomical arrangement which is constant. As there are many different forms of white fibrous tissue distinguished from each other by the arrangement and general character of the fibrous tissue and by the manner in which it was produced, so we find a corresponding diversity of structure and difference in mode of production in the tissues which fall into the group of *elastic tissues.* The parallel fibres of the ligamentum nuchæ, of the vocal cords, of the ligamenta subflava, and other pure elastic ligaments, differ widely from the lax network of long fine fibres of elastic tissue present in the areolar tissue beneath the skin and mucous membranes, amongst muscular fibres, connected with nerve fibres, &c. Both these

forms are totally unlike the thin delicate longitudinal fibrous layer which lies just beneath the epithelium of an artery, and this again differs in important characters from the elastic tissue beneath it.

The circular fibrous coat of the larger arteries contains a number of very coarse fibres, and in this situation is often seen a form of tissue which cannot be termed fibrous at all. The elastic structure seems to form a very coarse network which is often spread out in a membranous form with numerous spaces or holes in it. Mr. Quekett found that the large fibres of the ligamentum nuchæ of the giraffe exhibited transverse markings equi-distant from each other, almost like striped muscle. These marks are not to be seen in all the fibres, and they are most distinct in the oldest. They do not extend quite across the fibre, but appear to arise from a shrinking of the central part which causes it to break up transversely into smaller segments.

Fine elastic fibres encircle the bundles of fibrous tissue of tendon, and there are fine fibres which resist the action of acetic acid connected with the oval nuclei embedded in the fibrous tissue (nuclear fibres, Kernfasern). The first are probably the remains of vessels or altered nerve-fibres, while the last are not elastic fibres at all, as was pointed out when we were considering the anatomy of tendon.

FORMATION OF YELLOW ELASTIC TISSUE.

Kölliker's new views.—With regard to the formation of yellow elastic tissue, different views are entertained. In his "Manual," published in 1860, and in his former editions,

Prof. Kölliker states, that these fibres are formed from cells, and he has given a drawing of "stellate formative cells of fine elastic fibres from the tendo-Achillis of a newly-born child." He says, that "in all parts of the embryo which afterwards contain elastic tissue, peculiar fusiform or stellate and sharply-pointed cells can be recognized, which, by their coalescence,* produce long fibres or networks. The fibres not unfrequently persist in this condition of stellate anastomosing cells, or connective tissue corpuscles (Virchow), as—*e.g.*, in the tendons and the cornea, in ligaments and ligamentous discs, in the corium, in mucous membranes," &c. He also, with Virchow, considers these cells and fibres on a parallel with the canalicular systems of bones and teeth, and proposes to call them *plasm*-cells, and their processes *plasm*-tubes, because they are supposed to convey nutrient juices.

Last year, however, Prof. Kölliker completely abandoned his former views as to the fibres being formed from cells, and now maintains that the cells or nuclei which exist in such number at an early period of development have nothing whatever to do with the formation of the elastic fibres. He differs from Virchow as to the relation of the elastic fibres to the cells, and, so far from believing that they are continuous, maintains that the

* It is doubtful if cells *ever coalesce* during the development of tissue. Cells divide, and the subdivisions *separate* from each other—a fibre in many cases extending between them. This fibre of course increases in length as the cells become separated farther and farther from each other. Cells do not coalesce, nor do tubes or processes grow from them and coalesce with tubes or processes from neighbouring cells.

yellow elastic tissue corresponds to *intercellular substance.* In the development of the ligamentum nuchæ he says that the cells seen at an early period of development assist in the formation of an interstitial substance, "from which by independent differentiation both the connective tissue and the elastic fibrous networks proceed." By this term "differentiation," I conclude Prof. Kölliker means that from an interstitial substance originally homogeneous, connective tissue and yellow elastic tissue separate or are deposited just as we may obtain from the same clear solution containing certain substances, definite compounds having totally different forms and chemical properties.

The Author's observations.—I have already shown that the apparent fibres (Virchow's tubes) which resist the action of acetic acid and are embedded in the substance of the tendon, are not composed of elastic fibres at all, but merely consist of imperfectly formed tendon which, like other tissues at an early period of formation, resists the action of acetic acid. The formation of these apparent fibres is therefore to be accounted for without supposing that like the gelatine-yielding fibrous tissue in which they lie, they result from the "differentiation" of an intercellular substance. It is not possible, nor would it be advantageous, to consider fully this long and very complicated question; but with regard to the ligamentum nuchæ, I would remark—

1. That even in the adult ligamentum nuchæ (sheep) nuclei (masses of germinal matter) are continuous with the material of which the yellow elastic tissue is composed.

2. That these nuclei bear to the thick elastic fibres pre-

eisely the same relation whieh the nuelei of tendon bear to the white fibrous tissue.

3. That in the ligamentum nuehæ of the young sheep, fibres of different age and size may be obtained. The mode of development of the fibres may, in faet, be studied as well as in an embryonic tissue.

4. That therefore in all eases the elastie substanee results from the gradual eonversion of germinal matter into this strueture, and in the ligamentum nuehæ and other parts where yellow elastie tissue is formed in quantity, the tissue is eontinuous with the masses of germinal matter, and never results from the differentiation of an intereellular substanee. The germinal matter passes gradually into fully-formed tissue, and the oldest portion of the tissue is that whieh is most distant from the germinal matter, as in other eases.

5. What appears to be an individual fibre of sueh a tissue as the ligamentum nuehæ is not so. It may be readily torn into very mueh finer fibres. In the ease of young fibres, the nuelei are observed to be wider than the fibres themselves, for, after the elastie tissue has been formed it gradually beeomes eondensed, loses water, aud the diameter of the fibre must neeessarily be less than that of the nueleus up to a eertain period of its growth. As the fibre grows in thiekness the nueleus is seen at its side just as in tendon. One of the thiek fibres of the ligamentum nuehæ with nueleus, therefore, eorresponds to one of the small bundles of fibrillated tissue of tendon with its nueleus.

Fibres of elastic tissue not formed directly from nuclei.—We have already seen that there are fibres elosely resem-

bling elastic tissue embedded in a delicate transparent matrix with undoubted nerve-fibres, and we were able to trace fibres in various transitional conditions, from the nerve-fibre to a structure resembling a fibre of elastic tissue, so that there are in mucous membranes, the papillæ of touch and taste, outside the sarcolemma of muscle, and in other tissues, fine fibres, forming networks closely resembling the fibres of elastic tissue in general appearance, which are not formed from cells or nuclei, but which must be regarded as the remains of tissues which were functionally active at an earlier period of life, especially nerve-fibres and vessels (see my paper on the "Distribution of the Nerve-fibres to the Mucous Membrane of the Epiglottis of Man," Archives of Medicine, No. XII., page 250; and "Lectures on the Structure of the Simple Tissues").

CERTAIN CHANGES OCCURRING IN FIBROUS TEXTURES IN DISEASE.

In health the normal changes occurring in fibrous tissues seem to consist of the gradual increase in the quantity of the fibrous formed material, and the condensation of that which has been already produced. The fibrous tissues of the adult and of aged persons contain a higher percentage of solid matter than those of the child.

The changes above referred to occur very slowly, and it is probable that very slight, if any, absolute disintegration and complete removal of white and yellow fibrous tissue takes place during life in the healthy state. These tissues are supplied with a very small proportion of nutrient

matter, and the germinal matter is very slowly converted into fibrous tissue. But the fibrous material to retain its healthy state must be permeated in every part by fluids, which slowly pass to and from the nuclei. In certain cases fatty matters are precipitated from the fluids amongst the fibrous tissue, or amongst the masses of germinal matter, and in consequence the tissue deteriorates. In the low form of soft fibrous tissue in the umbilical cord, and in the placenta, this change is seen towards the termination of the period of gestation. Very numerous oil globules and pigment granules are deposited amongst the fibres and precipitated amongst the particles of germinal matter. No such appearances are observed in the earlier periods, when the formation of tissue is actively taking place. In the higher forms of fibrous tissue corresponding changes are observed in advanced age—changes which are so constant that we are almost entitled to consider them as occurring normally; but in persons of healthy and vigorous constitution they are postponed to a much later period of life than in those whose nutrient processes have been impaired by disease and modified by the altered composition of the nutrient fluid. We have many opportunities of observing such a change in the case of the cornea. I have seen the arcus senilis remarkably distinct in a man of forty years of age, while I know an old lady of upwards of ninety-eight in whose cornea the change appears only to have recently commenced.

Whether these changes result from the power of the nuclei being impaired or from an alteration in the composition of the fluids which are transmitted to the nuclei, cannot

be discussed here; but I may mention that various facts seem to favour the latter of these views, for, as my friend Mr. Edwin Canton has shown, corresponding changes occur in many other tissues of the body. That such changes do not in all cases lead to fatal results is no more than would be expected, but this does not in any measure diminish their significance. Arcus senilis never occurs at the age of forty in strong vigorous constitutions, and it is very seldom fully developed in persons who have lived very carefully, or who have weak stomachs, and therefore compelled to do so, at the age of fifty or sixty.

Of the death of the tissue—Suppuration.—When the vitality of the nuclei of fibrous textures is destroyed, either from their not being supplied with nutrient matter, or in consequence of being bathed with fluid of an abnormal nature, the fibrous tissue becomes softened and undergoes decomposition, and the dead portion is detached—in fact, sloughing takes place. On the other hand, if the germinal matter (nuclei, connective tissue corpuscles) be supplied with an increased quantity of nutrient matter, owing to the fibrous tissue being rendered more permeable or otherwise modified; at first there exists a tendency to the formation of new elementary parts (germinal matter and connective tissue), but if the change once commenced, increases, the germinal matter multiplies so rapidly that no formed material is produced. There is not time for the formation of any fibrous tissue whatever—in truth, the process of suppuration is established. Those soft connective tissues which contain the greater number of nuclei (masses of germinal matter), and are most freely supplied

with bloodvessels, and receive a large proportion of nutrient matter, are most liable to suppuration. The process of suppuration is, on the other hand, often arrested by a living fibrous tissue—as tendon or fascia—this fibrous tissue resists the tendency of the pus corpuscles to grow at its expense, and while softer and more succulent tissues are destroyed, it retains its vitality.

LECTURE VII.

ADIPOSE TISSUE—CARTILAGE.

Adipose tissue—Supply of bloodvessels—The fat cell or vesicle—Of the formation of fat and the development of the fat vesicle—Formation of fat in the cartilage cell and the liver cell—Tumours consisting of adipose tissue—Cartilage—Structure of cartilage—Formation and growth of cartilage—Changes occurring in fully-formed cartilage—Minute structure and development.

Adipose tissue.—Adipose tissue is generally associated with areolar tissue, and the fat vesicles lie in the spaces which exist in the areolar tissue. These spaces can be distended artificially with air or fluid. In cases of general emphysema air accumulates in the areolar tissue, and in œdema and anasarca serous fluid occupies the areolæ of the areolar tissue. There are certain localities, however, in which, even in very corpulent people, areolar tissue exists without adipose tissue; for example, in the eyelids, between the rectum and bladder, in the median line of the abdomen, beneath the skin of the scrotum and penis, in mucous membranes, and in some other situations, areolar tissue exists without adipose tissue. In the medullary cavity and in the cancelli of the cancellated structure of bones of mammalian animals adipose tissue is said to exist without areolar tissue. Although marrow is undoubtedly a very pure form of adipose tissue, some fibres of areolar tissue can almost always be detected in it.

Supply of bloodvessels.—Adipose tissue is generally freely supplied with bloodvessels, and in an injected specimen you find the capillary vessels arranged so as to form the boundaries of spaces varying a little, but not very much, in size. Each space contains a fat cell or vesicle, which is the "elementary part" of adipose tissue. In the frog, in fish, and many of the lower animals, and in man, mammalia, and birds, during development, the meshes of the vascular network are much wider, so that many fat cells lie in one space. In man and mammalia, however, the vessels are very numerous, and grow as the fat vesicles increase in number. At the margin of a collection of vesicles the changes taking place during the increase of the adipose tissue may be studied.

The fat cell or vesicle.—The fatty matter in adipose tissue is always situated within a very thin membrane, vesicle, or closed envelope. Indeed, the envelope is a good example of a *cell-wall*, and its presence is constant, but its true significance and the mode of its production can only be understood by carefully studying the changes occurring during development. The young fat cell has neither fat nor cell-wall! The form of the adult fat vesicle is spherical or oval, and often exhibits many flattened sides from the pressure of contiguous vesicles. It varies much in size, but its characters can be well studied in a fat pig. In human fat, the hard crystalline fat, generally termed margarine, crystallises and separates from the more oily or fluid fat after the adipose tissue has been preserved for some time.

The formation of fat and the development of the fat vesicle.—The development of the fat cell and the for-

mation of the fatty matter are points of considerable interest. The fat is formed and deposited in the substance of the granular material of which the fat cell is in its early stage composed. The deposition of the fatty matter may be compared with the deposition of starch and some other "secondary deposits" found after a certain period of growth has been reached in some vegetable cells. But the fatty matter is not only deposited from a solution—it is *formed.* Fat may be produced in a fat cell, although no fatty matter has been taken in the food, and there is reason to believe, even where no oily material exists, dissolved in the particular fluid from which the fat cell draws its nutrient materials. And in cases where fat does exist in the pabulum, the composition of the fatty matter of the tissue is very different from that of the fatty matter of the food; nay, more than this, the fats of man, of the ox, sheep, rabbit, and other animals, differ from each other in most important characters and in chemical composition; neither is their composition very simple, for several different fatty acids exist in combination in one kind of fat. We should expect to find these specific differences just as we find differences in the composition of the blood, milk, urine, &c., of different animals, which in some cases are closely allied to each other in zoological characters.

At an early period of development, we observe a number of oval or spherical masses of germinal matter (nuclei) in those positions where fat is to appear. These divide and subdivide, as in the development of other tissues. The collection is freely supplied with capillary vessels. If the tissue be stained with carmine, each mass is coloured

darkly in the central portion (nucleus), and external to this there is a layer of granular matter only faintly coloured. The latter gradually increases, and amongst the granules a number of small oil-globules make their appearance, or only one is to be seen. This is the first appearance of fat, and it is *formed* in the substance of the granular matter external to the nucleus. The fat gradually increases and soon occupies the greater part of the "fat cell," which now consists of a large globule or several small globules of fatty matter, and a thin layer of granular matter around this, which is much thicker in one spot than elsewhere, and there the original nucleus is situated. The granular matter undergoes condensation at its outer part, and becomes the clear transparent cell-wall or vesicle, and in the fully-formed fat cell the nucleus will be situated between the fat and the wall of the cell. As long as the nucleus or mass of germinal matter remains the fat may go on accumulating in the interior.

Formation of fat in the "Cartilage Cell" and "Liver Cell."—Now, how is the fat formed? It seems to me clear that some of the granules, of which the granular matter is composed, become resolved into fatty matter, and perhaps other substances, which, being soluble, pass away from the cell. The fat is not deposited upon the outer part of the granular matter, nor quite close to the nucleus. The outermost portion (the oldest) becomes condensed to form "cell-wall," and that within this gives rise to the fat. The "matrix" in which any forms of "cells" exist, corresponds to the "cell-wall" of a fat or other "cell." Nor is it only in true adipose tissue that such changes occur.

In the interior of the so-called cartilage cell and liver cell fat is formed in the same manner. Thus the cavities of cartilage may be occupied with fatty matter, as well as a nucleus. Large oil globules may be seen in the substance of the matter of which the body of the "liver cell" is composed. Indeed I have seen many "liver cells" which could not be distinguished from the "fat cells" of normal adipose tissue, and in extreme cases of fatty liver, were it not for the arrangement of the vessels, a thin section could not be distinguished from one of adipose tissue. This was remarkably the case in a liver which I examined many years ago for Dr. Budd. It contained 65·19 per cent. of pure fat.*

In many of the lower animals some of the liver cells become converted into fat cells, and at length ordinary adipose tissue is formed, while others continue to be developed as liver cells, their formed matter being resolved into biliary and amyloid matter.

It is very interesting to compare the changes taking place in the fat cell with those occurring in the starch cell of a plant. First, in each case, we have a layer of granular matter around the "nucleus." The outermost part in each case becomes the "cell-wall;" a layer within this, in which the nucleus is embedded, is the seat of deposition of the fat in the one case, and the starch in the other. This layer is called the "primordial utricle" of the plant cell, and exactly corresponds to the layer of granular matter around the fat, which is faintly coloured with carmine, in

* "Diseases of the Liver." Dr. Budd. 2nd Edit., p. 281.

specimens of young adipose tissue, which have been thus prepared. The adipose tissue of the frog is very favourable for studying these important changes. The results described illustrate the great importance of investigating the changes occurring in tissues from their first appearance, and of comparing the changes occurring in vegetable with those of animal tissues. I have endeavoured to show that the starch of the vegetable cell corresponds in position to the fat of the fat cell, and both substances may be said to result from changes occurring in the particles of germinal matter. The particles of germinal matter end their existence by breaking up into certain substances, and starch and fat being insoluble cannot escape, and continue to accumulate in the cell as long as the germinal matter continues to be produced.

Tumours consisting of adipose tissue.—Adipose tissue, which could not be distinguished from the normal structure, frequently forms a morbid growth. Many of the fatty tumours seem to consist of an unusual formation of adipose tissue at one particular spot, and such tumours often attain an enormous size; in fact, having once commenced, they continue to increase as long as they are supplied with nutrient matter. It would seem that, in such cases, the conditions which in the normal state cause the formation of adipose tissue to proceed regularly and uniformly, are absent in one particular spot where the growth of the tumour commences. Tumours consisting of this structure usually originate in adipose tissue. There are several kinds of fatty tumours, so-called, which do not consist of adipose tissue.

CARTILAGE.

Structure of cartilage.—Cartilage is one of the most important of the tissues which have been arranged in the series of connective tissues. The greatest differences of opinion exist as to the essential structure and mode of formation of cartilage. It is generally supposed that cartilage consist of *cells* and an *intercellular substance*, and it is maintained by many that each cartilage cell possesses a very thin wall or capsule, distinct and separate from the cartilage matrix. By others, it is considered that the soft granular matter, just within the cell-wall, corresponds to the primordial utricle of plants—so that we may have passing from within, outwards, *nucleus*, *certain cell contents* (as not unfrequently *fatty matter*), *primordial utricle*, *external cell membrane;* and distinct from the latter, supposed to be deposited independently of it, the so-called *intercellular substance*. When these views are applied to the many different forms of cartilage, fibro-cartilage, and embryonic cartilage, the greatest difficulties are experienced. Thus, the cell-wall cannot always be demonstrated as distinct from the matrix. Sometimes there is no proper matrix at all. In certain forms, fibres, resembling those of yellow elastic tissue, exist in the position of the intercellular substance, and in fibro-cartilage the *intercellular substance* resembles white fibrous tissue.

The so-called primordial utricle or the "protoplasm" sometimes seems to be continuous in structure with the cell-wall, sometimes distinct from it. The capsules or cell-walls sometimes pass gradually into the intercellular

substance, and as these are formed one within the other from the cells,* the latter must, therefore, at least take part in the formation of the intercellular substance; but in some instances it is maintained that this is formed without the agency of the cells. I might adduce very many conflicting statements with regard to the anatomy of the simplest form of cartilaginous tissue, but such a course would not be advantageous in a series of lectures like the present. I shall follow the same plan as in other cases, and describe the appearances I have observed myself, and which I hope to be able to show you in my next demonstration of microscopical specimens. I shall presently describe, somewhat in detail, the changes which can be observed during the formation of one kind of cartilage.

Formation and growth of cartilage.—All observers are, I believe, agreed that, at an early period of development, cartilage consists almost entirely of what have been termed "cells," but these "cells" have no distinct cell-wall, and the granular matter of which they are composed is continuous with the soft transparent material in which they lie, or which forms a thin layer between them. Now, if I discuss what, is *nucleus*, what, *cell-contents*, what, *cell-wall*, what, *intercellular substance*, I shall very much increase the difficulty you will meet with in endeavouring to form a notion of the history of the changes which take place in the formation of cartilage. But, as it is literally true that every form of cartilage consists at an early period of

* See a paper on "Connective Tissue," by Dr. Martyn, in my "Archives," vol. ii., p. 110.

roundish masses of granular matter (germinal matter), embedded in a small quantity of soft transparent formed material, it is only necessary to investigate carefully the alterations which occur during development in this simple typical structure. As in other cases, in the perfectly fresh tissue the germinal matter is continuous with the formed material. Sometimes, after death there is an appearance as of masses with a well-defined outline distinct from the formed material, and hence has arisen the notion of cells with distinct cell-walls. Any mass of germinal matter placed in water exhibits a sharp outline, and this has been considered to indicate the existence of a cell-wall.

The masses of germinal matter at first are very close together; they divide and subdivide as they lie in the soft formed material, and, as development proceeds, become separated from each other by gradually increasing intervals. At the same time, the formed material undergoes slow condensation, and the formation of new formed material on the surface of each mass of germinal matter more than compensates for the shrinking of the matrix, which would otherwise be manifest. Each of these masses of germinal matter divides and subdivides, and formed material is produced on the outer surface of each, so that there are small collections of masses of germinal matter separated from each other by a considerable extent of formed material in the shape of fully-formed cartilage, while the separate masses composing each collection are themselves separated from each other by a very thin layer of recently produced and much softer formed material. Thus the gradual condensation of the first produced

formed material proceeds without shrinking of the entire mass, and without the formation of large cavities. The division and subdivision of the original masses of germinal matter proceeds, and new formed material is formed, but more and more slowly, as the condensation of that already produced goes on. For some time the entire mass continues to increase in bulk, and at the same time becomes less permeable to nutrient fluids.

Changes occurring in fully-formed cartilage.—The formation of cartilage tissue even continues in adult cartilage, although the entire mass may undergo no alteration in size, for as the tissue advances in age it undergoes condensation. Slowly indeed are these changes carried on, but the slowness of the changes results from the slightly permeable nature of the "matrix." The germinal matter still has the *power* to grow rapidly, and it will grow rapidly if the cartilage become more permeable to the fluids, or if the access of the pabulum to the germinal matter is facilitated by artificial means. As in other cases the rapidity of the growth of germinal matter simply depends upon the supply of pabulum. Let a thread be passed through a healthy cartilage, so as to make artificially a channel by which the pabulum may reach the masses of germinal matter more quickly, and the operation will be very soon followed by the division of the masses of germinal matter. The formed material in their immediate neighbourhood will be softened, and may even be appropriated by them. This state of things continuing, pus may result, or the masses of germinal matter not multiplying so fast as is involved by this supposition, may give rise to the formation

of a soft pulpy formed material, like that of embryonic cartilage at an early period of development. These changes do not result, as is generally believed, from "*irritation*," or from the cells being "*stimulated*" to take up more nutrient matter within a given period of time than in the normal state, but they depend simply upon the restrictions to the access of the pabulum to the germinal matter being to some extent removed.

Minute structure and development.—Now, let me ask your attention to the minute anatomy of one form of permanent cartilage, in order that I may demonstrate to you the appearances which are actually observed, and which, I believe, can only be accounted for according to the simple view I have proposed. As the masses of germinal matter are very large and their arrangement distinct, and as specimens may be obtained every where and at all seasons, I will take the cartilage of the common frog. In the diagram are represented different parts of the cartilage in different stages of growth, and you shall see the actual specimens from which the drawings have been taken in my next demonstration. The germinal matter is distinguished from the formed material in each case by the colour produced by the alkaline solution of carmine. The different drawings represent the cartilage in different stages of growth.

At *a*, large oval masses of germinal matter are seen to be separated from each other by a very thin layer of soft formed material (matrix), which is slightly granular, but not coloured by the carmine solution. At *b*, the mass of germinal matter has increased in size, but as the latter

substance grows, while, at the same time, the conversion of its outer portion into formed material proceeds, the entire elementary part, consisting of germinal matter and surrounding formed material (cell and corresponding portion of matrix) becomes larger. The next stage is shown in *c*. Several zones, exhibiting different shades of colour, are now seen; the outer one, which passes into the formed material, being the most faintly, the innermost portion of the germinal matter (nucleus), the most darkly, tinted, although to reach this the solution must have passed through all the outer layers. In *d*, *e*, *f*, *g*, *h*, *growth* of the entire elementary part seems to have ceased, but the conversion of the oldest part of the germinal matter into formed material proceeds, until at last only what is termed the nucleus remains, and this in many instances dies and a small oval collection of granules, which are not tinged red with carmine, *h*, is all that marks the position of the mass of germinal matter by which the surrounding matrix, or formed material, has alone been produced. After this has occurred the matrix may become harder and undergo other changes, but no more can be formed. The *formation* of the matrix in this particular spot has ceased. The matrix, close to the germinal matter which is recently formed, is of course soft, and when it is broken away the mass of germinal matter within, escapes entire. In all tissues the bond of union between the germinal matter and formed material is very slight; a fact which receives a simple explanation upon the view of growth brought forward.

The formation of cartilage is generally described in a very different manner. It has been said that the mem-

branous eapsule of the eartilage eell *sends in septa* when the eells it contains undergo division "whieh serve as new envelopes for the young eells, yet in sueh a way, that even the gigantie groups of eells, whieh proeeed from eaeh of the original eells, are still enelosed in the greatly enlarged parent eapsules." (Virehow.)

Against this theory I have endeavoured to show that the matrix or intereellular substanee with the membranous eapsules of the eartilage eells eorresponds with the eell-wall of a spore of mildew. It does not possess formative power. It *has been* produeed. It has been formed, but it is now passive. It may be added to, but it eannot inerease or build itself up out of pabulum. The outer eapsule of the mildew, as I have tried to prove, does not possess inherent powers of growth. It is the internal germinal matter whieh is alone eoneerned in the growth of the plant. So in eartilage, the matrix was onee in the state of germinal matter. The septa do not *extend themselves in, or grow in*, but the material of which they are eomposed results from an alteration taking plaee in the oldest partieles of the germinal matter.

In eonelusion, let us eonsider how the matrix of eartilage is produeed. It is eertain, from the above observations, that the matrix is never produeed without the masses of germinal matter, nor ean it inerease without these. In disease ehange is observed in the rate of growth of these masses. After the matrix is produeed many of the masses of germinal matter may die and disappear, but in growing eartilage they are invariably present. I have endeavoured to prove that granular matter, of whieh the germinal

matter consists, is always directly continuous with the more or less transparent matrix, and that this granular matter becomes converted into the matrix. There is no appearance of a cell-wall distinct from the matrix, nor is there an interval between the granular matter and the matrix, unless post-mortem change has occurred. The first passes uninterruptedly into the last. The ragged outline of many of the masses of germinal matter in the cartilage from the frog renders the terms "cell nucleus," "cell contents," or "granular corpuscle," totally inapplicable, and it is clear that to such masses there could be no cell-wall. The germinal matter, therefore, gradually *becomes* the matrix, and all matrix was once in the state of germinal matter, as all the matter in the living or germinal state was once in the condition of pabulum. Without germinal matter there *can* be no cell-wall or intercellular substance. In all cases pabulum is converted into germinal matter by preëxisting germinal matter, and germinal matter is at length converted in formed material, be it fluid or solid, cell-wall, secondary deposits, or intercellular substance.

We shall find when we come to consider the anatomy of bone, that the first deposition of calcareous particles takes place in the formed material at a point midway between the masses of germinal matter—that is, in *the oldest portion* of the formed material. The deposition of the calcareous matter can be explained by physics, and can be imitated out of the body, but the matrix which is formed cannot be produced artificially. This results from changes occurring while the matter of which it consists

was in the state of living germinal matter. In several specimens I shall show you, you will see that the fibrous tissue of tendon is continuous with the matrix of the cartilage, and you may trace the gradual transition from the clear transparent cartilage matrix to the fibrous tissue of the tendon. So, the contractile material of muscle is continuous with the fibrous tissue of tendon, and the so-called nuclei in the two tissues exactly correspond. The formed material in each tissue is continuous, and the masses of germinal matter bear to it a similar relation. The *formation* of cartilage, tendon, or muscle depends—1, upon the vital powers of the germinal matter which becomes converted into these tissues; and it is influenced, by 2, the conditions present while this conversion is occurring.*

* See also a paper "On the formation of the so-called Intercellular Substance of Cartilage, and of its relation to the so-called Cells, with Observations upon the Process of Ossification," in the "Trans. of the Microscopical Society," No. XII., October 1863.

LECTURE VIII.

BONE.

Bone composed of organic matter and inorganic matter—Of living bone and dried dead bone—An elementary part or cell of living bone—An elementary part of dried dead bone—Of the formation of the lacunæ and canaliculi of bone—The views of Virchow and Kölliker—Canaliculi not processes of a cell—The relation of the vessels to bone—Of "myeloid cells," and of the formation of the plates and spiculæ of the cancellated structure. Of cancelli and of Haversian canals and spaces—Of form, structure, and chemical composition—Of the periosteum, and of the so-called medullary membrane—Of the medulla or marrow of bone—Of the development of bone—Of ossification in fibrous membrane—Ossification in temporary cartilage—Of the growth of a long bone in length and circumference—Of the germinal or living matter of bone—On necrosis, caries, and mollities ossium—Of the germinal or living matter of bone—Of caries and necrosis.

There is no tissue in the organism the structure of which has been more carefully investigated than bone. Nevertheless, there still remains much to be determined, and many very different opinions are now entertained as to the structure and mode of formation of this tissue, and the views held by some observers are quite incompatible with the doctrines taught by others.

Bone differs from any other texture which has yet come under our notice in this important particular: that the formed material is impregnated with calcareous salts in such quantity as to produce a very hard unyielding tissue,

which, however, possesses a certain amount of elasticity. Hardness may be brought about in two ways in tissues: 1, by the slow condensation of an organic material resulting from a gradual process of drying, as is the case in *cuticle*, *hair*, *nail*, *horn*, *&c.*; and 2, by the deposition of hard inorganic matters in a soft organic matrix, as occurs in the case of *shell*, *bone*, and *teeth*.

You may actually have bone tissue produced, but in consequence of this secondary process of calcification not having occurred, it remains perfectly soft and useless for the purposes for which bone is required. We shall see that the production of the soft bone tissue is *one process*, and the precipitation of lime salts in, and their incorporation with, the soft matrix, *another process*. The first cannot be produced without *vital actions*. The last is due to chemical changes, and can be, to a certain extent, imitated artificially. In the formation and growth of bone we can distinguish with great precision the results of the vital processes from the effects of the purely physical changes.

It is easy to prove that bone consists of soft tissue impregnated with hard calcareous matter. You may obtain the soft organic matter by steeping a bone for some time in dilute hydrochloric acid, for this acid dissolves the calcareous salts, and leaves the tissue of the bone. This decalcified tissue is so soft that a long bone treated in this way may be bent or even tied in a knot, yet every eminence, every minute canal, and even the slightest inequalities of the surface are as distinctly marked as before the action of the acid. Upon the addition of excess of ammonia to the acid solution the calcareous salts are pre-

cipitated in an insoluble form, and by applying appropriate tests we may detect phosphates of lime and magnesia, a little carbonate of lime, with traces of fluoride of calcium.

Again, the calcareous salts of the bone may be made evident by another process which causes the destruction of the organic matter. If a bone be subjected to a red heat it becomes charred and black, but if kept for some time at this high temperature exposed to the air, the carbon is all burnt off, and escapes as carbonic acid, while the calcareous salts remain behind in a pure state. If the process is conducted with care, although the bone shrinks a little, its form is unaltered, and every eminence and every hole is as distinct as in the recent bone, and the bone treated with acid.

Of living bone and of dried dead bone.—The authors of our manuals and treatises on minute anatomy usually describe the structure not of *living* or *recently dead bone*, but of bone which has actually been *dried*. This gives to the student a notion of the structure of bone as imperfect and incorrect as that which he would form of the structure of skin, nerve, or muscle, if he were to examine dried specimens of these tissues. We ought to endeavour to teach the structure of tissues as they *live*, *grow*, *and decay in living bodies;* but every anatomical work with which I am acquainted describes not the bone in the state in which it exists in the body, but bone which has been dried and deprived of its *living matter*. The same highly objectionable course is always followed also with regard to the tooth structures; and I believe to this system is mainly to

be attributed the difficulty of giving to the student a correct notion of the structure of these tissues.

I shall commence by describing an elementary part or "cell" of bone, then I shall consider the changes taking place in the formation of this elementary part. Afterwards we shall be in a position to discuss the anatomy of the so-called *cancellated structure* and *compact tissue of bone*, and study the changes occurring in the course of *development* of mammalian bone.

An elementary part of living bone.—An elementary part of *fully-formed bone* consists of a mass of germinal matter, surrounded on all sides by, and continuous with, a thin layer of soft formed material, which passes uninterruptedly into the hard calcified formed material (*matrix or intercellular substance of authors*). This hard material is penetrated everywhere by very fine channels (*canaliculi*) through which the nutrient material passes towards the masses of germinal matter.

An elementary part of every kind of bone at *an early period of its formation*, consists of a mass of germinal matter, surrounded by a certain proportion of granular, homogeneous or more or less fibrous formed material. This last becomes the seat of deposition of calcareous matter, which proceeds from *without inwards*, and the formation of the canaliculi takes place in the same direction; for I shall show, in opposition to the generally received opinion, that the formation of these tubes commences not at a point nearest to the germinal matter or "cell," as is affirmed, but at a distance from it.

An elementary part of dead dried bone.—An elementary

part of fully-formed *dead* and *dried bone* consists of a *space (lacuna)*, occupied in the recen t state with germinal matter. Numerous pores or channels *(canaliculi)* pass in a tortuous manner from one lacuna to adjacent lacunæ. In the dry bone the lacunæ and canaliculi are both occupied with air, and in consequence of the great difference in refractive power between the air and the transparent bone tissue, the light is so bent out of its course in passing from one medium to the other, that the cavity and tubes appear *black*, just as a small air bubble in water looks like a mass of dark solid matter. From this solid appearance the cavities, with the enclosed air, were once called "bone corpuscles."

The channels (canaliculi) of one elementary part of bone communicate with those of adjacent elementary parts, so that if a thin section of dry bone be moistened with turpentine, or thin Canada balsam, at one part of the specimen, this penetrating fluid may be seen to run up the canaliculi into the nearest lacunæ, and from the latter spaces it passes to all the neighbouring canaliculi and lacunæ. The refractive power of the turpentine so nearly corresponds to that of the osseous tissue, that the whole section appears homogeneous, and you can with great difficulty discern either lacunæ or canaliculi :—so different are the appearances produced in the same dead dried tissue by different processes of examination.

The difference between dead bone and living bone is this—that in the first the *formation* of bone tissue has everywhere ceased, while in the last it is still proceeding, and around each mass of germinal matter the *formation*

of matrix and the deposition of calcareous salts in the matrix already formed is going on. These changes may be occurring very slowly, but in all living bone they are taking place, so that the only matter in a living bone which is actually *alive* is what is ordinarily termed the "*nucleus*" or the "bone cell" in the space or lacuna; but the fully-formed osseous tissue around is, I believe, to all intents and purposes, as devoid of life while the bone yet remains in the living body, as after its removal. This small mass of germinal matter, perhaps not more than one-twelfth of the bulk of the bone tissue corresponding to it, is the only portion which possesses active powers. It alone can *grow* and give rise to the *formation of matrix*. Bone cannot *produce bone*, but the *germinal matter* of bone may become *converted into new bone tissue*. . . . .

Of the formation of the lacunæ and canaliculi.—What then is the simple anatomical element of bone, the elementary part which corresponds to a cell of epithelium for example? Virchow says bone contains, "in an apparently altogether homogeneous basis-substance, peculiar stellate bone cells, distributed in a very regular manner."

According to this view it is maintained that the matrix is formed as a true *intercellular* substance, while from the "cells" proceed processes which grow into the matrix and anastomose with those from neighbouring cells. The "lacuna" is occupied with a "cell" with stellate processes which pass into the canaliculi. The conclusion to which my observations have led me is very different; and the elementary part of bone would consist of the *germinal*

matter with the osseous tissue and canaliculi around it, extending as far as the point midway between adjacent lacunæ.

In order to form a correct notion of the structure of bone, it is necessary to study the changes taking place in simple cartilage during its conversion into true bone. In the frog the various changes may be accurately observed from the earliest existence of the cartilage to the formation of the perfect bone, and at no period of development can stellate cells, *with processes corresponding in number to the canaliculi*, be separated, as has been described. The matrix is not formed independently of the cells, nor do stellate cells, the processes of which anastomose together, exist at all.

The diagram shows the manner in which the earthy matter is deposited in the matrix of cartilage. It is copied from a section of the temporal bone of a frog. Globules of earthy matter may be seen to form imperfect rings around the cartilage cells. The calcareous matter is always deposited in the matrix (formed material) at a point midway between adjacent "cells," that is, in the *oldest portion of the formed material* of the cartilage. The deposition gradually proceeds *from without, inwards*. The outer part of the germinal matter of the cell gradually undergoes conversion into matrix, which in its turn becomes impregnated with calcareous matter until only a small space remains in which the nucleus still exists.

The different stages may be traced readily in frog's cartilage, and in many specimens, rounded globules of calcareous matter which coalesce and undergo great change

in form, can be demonstrated without difficulty in lacunæ in an advanced state of formation. Mr. Rainey has watched this process and seems to consider that molecular alterations in the earthy particles are the essential changes to which the formation of bone is due, but in every one of the spaces which Mr. Rainey has figured, a mass of germinal matter, "nucleus," existed in the fresh specimen.*

I have examined the process of ossification as it occurs in various animals with the aid of carmine, and have always been able to demonstrate masses of germinal matter in a position corresponding to the lacunal space. I believe these masses of germinal matter to be as necessary to the production of bone as they are to the formation of every other tissue, and feel certain they are constantly present, and that through their agency alone, osseous, as well as all other tissues, is formed. They are not directly concerned in the deposition of the calcareous matter, but the matrix in which this is deposited cannot be formed without them, and it is probable that by their instrumentality alone the regular circulation of fluids holding the calcareous matter in solution is maintained, and thus the extreme regularity with which the growth of the tissue occurs, is ensured.

For some time after the first deposition of the calcareous matter in the formed material, very thin fragments of the bone torn away exhibit the appearance of fibres (a fact pointed out many years ago by Dr. Sharpey), in the substance of which globules have been deposited, but slowly

* "On the Mode of Formation of Shells of Animals, of Bone," &c., Figs. 7 and 8, pages 118, 119.

the calcareous matter becomes more homogeneous, in consequence, probably, of changes occurring in its substance, and its more perfect incorporation with the organic matrix, and ultimately the hard mass appears even in texture, uniformly transparent, and penetrated everywhere by minute canals.

These tubes or channels are the altered spaces which are left between the calcareous globules originally deposited, and through them pass fluids to and from the germinal matter. They were at first triangular in outline, but gradually they have become altered by the filling up of the angles, until at last they become pores, the section of which is nearly circular.

From appearances I have seen in some preparations of the bones of the frog's skull (frontal, parietal), I feel sure that in this case the bone results from changes in the original cartilage. The nucleus of the cartilage cell remaining as the nucleus in the lacuna. The calcareous matter deposited in the matrix around a cartilage cell undergoes changes. It slowly becomes incorporated with the organic matter, and gradually ceases to exhibit the appearance of being composed of separate masses, and becomes more homogeneous. The spaces become canaliculi, and the mass at last assumes the structure of perfect bone. For some time separate calcareous particles are seen within the outline of the lacunæ, which gradually diminishes in size as calcareous matter is deposited in the matrix from without inwards. These views accord more nearly with those of Henle, who compared the formation of the lacunæ to the changes which occur in the walls of certain vegetable

cells through the secondary deposits of which pores are left, than with the opinion entertained by any other observer.

The views of Kölliker and Virchow.—Kölliker considers that the capsule of the cartilage cell and the matrix become impregnated with calcareous matter, while the granular cell corresponding to the primordial utricle of the vegetable cell, and with the endoplast of Prof. Huxley, remains within unaltered. He thinks that the canaliculi extend through the matrix by resorption.

Virchow regards bone as consisting of cells and an intercellular substance, and he considers the canaliculi to be processes which grow from the cells. In the following note, copied from page 417 of Dr. Chance's translation, he expresses himself very clearly as to the manner in which processes are formed from cells:—"The cartilage cells (and the same holds good of the marrow cells) during ossification throw out processes (become jagged) in the same way that connective tissue corpuscles, which are also originally round, do, both physiologically and pathologically. These processes, which in the case of the cartilage cells are generally formed after, but in that of the marrow cells frequently before, calcification has taken place, bore their way into the intercellular substance, like *the villi of the chorion do into the mucous membrane and into the vessels of the uterus*, or like the Pacchionian granulations (glands) of pia mater of the brain into (and occasionally *through*) the calvarium." Again, "the cells which thus result from the proliferation of the periosteal corpuscles are converted into bone corpuscles exactly in the way I described when speaking of the marrow. In the neighbourhood of the surface of

the bone the intercellular substance grows dense and becomes almost cartilaginous, the cells *throw out processes*, *become stellate*, and at last the calcification of the intercellular substance ensues."

There are few points in minute anatomy upon which such different views have been advanced as the one under consideration, and you cannot fail to notice that observers differ not only in the explanations and opinions they have put forward, but that there are irreconcilable differences in their statements of the facts. It is mere assertion to speak of the cells as throwing out processes, there are no facts whatever to justify such an inference.

Canaliculi not processes of a cell.—Although many observers have described and somewhat faintly expressed in their drawings the growth of the processes referred to, all agree that they are most difficult to see in healthy growing bone. My own observations compel me to oppose most earnestly the statements generally made with regard to these processes. As far as I have been able to see, neither the cartilage cell, nor the medullary cell, nor the periosteal cell, nor indeed any cell in the organism becomes stellate by the "shooting-out process." That cartilage and the other "cells" may become angular is perfectly true, and that a few little projections may be seen from different parts of their surface is also true, but these projections and angles have nothing to do with the formation of canaliculi, *nor do they correspond with them in number.* The appearance is exceptional instead of being constant, and a *lacuna with numerous canaliculi* may be produced without the *existence of an angular cell at all.* The mass of

germinal matter is oval from the period it first existed as a separate object to the time its nucleus is seen in the lacuna. Into each lacuna forty or fifty or more canaliculi open, and these communicate with those of adjacent lacunæ. Surely, if these were formed in the manner described we ought to be able to demonstrate something like this during the formation of the lacunæ, but nothing of the sort has been seen, and the warmest advocates of the theory have only been able to observe a very faint indication of the arrangement which they believe actually exists. Their drawings only show these processes projecting a very short distance from the cells, and no one, I believe, ever pretends to have seen processes from two neighbouring cells in process of communicating with each other, as exists constantly in the perfect canaliculi of bone. I would ask, why, if the tubes grow centrifugally from the cells they do not pursue the shortest route and pass in straight lines? By what force of attraction do opposite tubes come into contact, and how is the barrier interposed between the two, dissolved? But the impossibility of such a theory is shown thus, that it only accounts for the structure of the fully-formed bone *which is about to die*, and does not explain how the bone passes the earlier period of its life. It is not only very difficult to conceive such channels formed by an out-growth, but it is inconsistent with what is generally observed. The tissue *during its formation* requires channels, and it possesses channels, for the transmission of nutrient matter just as much as after its formation is complete. The portion of the canaliculus which is first formed is that which is most *distant*

from, not that which is nearest to the lacuna and its contents. The formation of canaliculi takes place in a direction *towards* not *from* the so-called "bone cell" or "nucleus."

If the canaliculi were formed as described it is quite impossible that every observer should have failed to see the prolongations of the cell undergoing development and coalescing with those of neighbouring cells. The extremities of these tubes which were gradually extending through the matrix would be rounded, and would contain germinal matter which would absorb the solid matrix, and thus the tube would extend through its substance. No such appearance has ever been seen. The canaliculi are no more processes of the cell which *bore their way* through the hard material than the canals which are left in the masses of secondary deposits in the hard walls of certain vegetable cells are processes of the germinal matter in the centre of the cell.

It may be said, if you please, that the growing matter extending from a spore of mildew bores its way into the soft material, at the expense of which it grows, but here this soft material is clearly appropriated by the mildew, and becomes converted into the germinal matter of the plant, but this process is totally different from that by which canaliculi are produced.

No stellate corpuscle has been produced, but the stellate appearance results from the circumstance that the calcareous matter has been deposited in the matrix in such a manner as to *leave intervals* arranged in a more or less stellate manner, as has been explained.

There is room for some difference of opinion with regard to the *contents* of the canaliculi. In dead dry bone it is certain they are simple tubes containing air. In *young* bone it is clear that all nutrient matter which reaches the germinal matter must permeate the matrix, and, therefore, there are no absolute "*tubes*" *at all.* This matrix must remain as the canal contracts by the gradual encroachment of the calcareous matter, and it is possible, and indeed likely, that after a time, by the constant passage of fluid, it may be gradually dissolved away, and thus a tube may result. But supposing it to remain, this portion of the matrix which occupies the canaliculi cannot be correctly termed "processes of the bone cell."

The relation of the vessels to bone.—The bony tissue with its canaliculi and germinal matter always has a certain definite relation to the vessels. It may exist as a simple thin lamina, covered upon each side with a highly vascular membrane, or as solid cylindrical processes often arranged so as to form a network, also invested with a vascular membrane; or the osseous tissue may be arranged in concentric laminæ around a central canal (Haversian canal), which in the living bone is occupied by a capillary vessel, around which are numerous fine granular cells. These cells are concerned in the removal of the osseous tissue. Each Haversian rod with its series of laminæ, and its capillary vessel in the centre, being about the one-five-hundredth of an inch in diameter. The diameter of the Haversian rods or systems varies, however, very greatly, some being less than the one-fifteen hundreth of an inch, while others are more than the one two-hundreth of an

inch in diameter. Of a thin plate of bone the tissue in the centre is the oldest. Of a solid cylinder, that in the centre was first formed, while of the laminæ of the Haversian system, those at the *circumference* are the oldest, and the laminæ close to the central vessel were the last developed. The first two forms of bony tissue constitute the cancellated structure, and the last (Haversian systems) make up the compact tissue of bone; but as you would suppose, transitional forms exist, and if you imagine thin laminæ of bone forming the boundaries of spaces, to be very much thickened by the formation of new laminæ within them, you approach the arrangement of the Haversian system; while, on the other hand, if the canal in the centre of several adjacent Haversian systems be very much increased in size, in consequence of the multiplication of the cells and the removal of the bone tissue, we should get an arrangement very like that seen in the cancellated texture. These differences are not fanciful, but such transitions can actually be demonstrated in almost all bones.

Of myeloid cells and of the formation of the plates and spiculæ of the cancellated tissue.—The little plates or cylindrical spiculæ of bone which enter into the formation of the cancelli are represented at first by soft masses, consisting of several elementary parts of bone. These masses may often be detached, and have the appearance of large compound cells, consisting of many smaller ones. They are found beneath the periosteum as well as in the medullary cavity, and in disease the soft spongy tissue which is formed in connexion with the bone consists of masses of

this kind. These are the so-called *myeloid cells*, which are composed of the anatomical elements, "cells" of bone. At this early period of the development of bone, the so-called myeloid cell consists only of several small oval masses of germinal matter, the outer part of each of which is undergoing conversion into the formed material. This gradually increases, and at a subsequent period becomes impregnated with calcareous matter, as has been already described.

In the diagram a good specimen of the so-called myeloid cells from one of the cancelli of the bone of the great toe is represented. Two or three of the masses are elongated and much bent. These might afterwards become ossified and give rise to the spiculæ of bone which form the imperfect septa between the cancelli. Around these are many small granular cells, and it is interesting to notice the fact, that while the first structures are of a dark-red colour the latter are scarcely tinged with the carmine, although both have been exposed to its influence in the same way. The first is growing actively, the last is comparatively inactive, and there can be no doubt that it is being gradually removed as the former structure advances. What remains will become the medulla, and many of the "cells" will become "fat cells."

Of cancelli and Haversian canals and spaces.—The elementary parts of bone are arranged so as to form the small cylindrical masses or plates, constituting the cancellated tissue, or more consolidated tissue, called the compact tissue, of which the shaft of a long bone is composed. It has been stated that in health a transition may always

be traced from the compact tissue to the caneellated strueture, and in disease, the eompaet tissue may bceome, and may be reprcsented by, this form of spongy bone strueture.

Now, not only does the compact tissue gradually pass into eaneellated strueture, but there are eomparatively largc spaees, like eancelli in the compaet tissue of a long bone. These are the *Haversian spaces* of Messrs. Tomes and Dc Morgan, who have proved most eonelusively that, during the life of the bone, canals are beeoming larger, and are eonverted into spaces by erosion. Absorption of the bone tissue takes plaee from within outwards, while in adjaeent spaees an opposite proeess is going on, and in the opposite direetion. The *formation* of bone takes plaee from without inwards, and an Haversian spaee gradually eontraets to form a eanal. The Haversian eanals and spaees are seen in a seetion of dry bone as openings, but in the reeent bone they are oeeupied by a vessel surrounded by soft pulpy tissue, eonsisting of a little conneetive tissue near the vessel, but mainly eomposed of small granular eell-like bodies. Sueh bodies are found on the deep layer of the periosteum and medullary membrane, as has been described. They are found in eonsiderable number wherever bone is being formed. These eells are the aetive agents in the proeess in all eases.

Now, the process of erosion or removal of an Haversian system does not take place quite regularly, for part of the Haversian system may be left while portions of neighbouring systems may be removed. When the formation of the new systcm eommenees in the spaee produced, it is obvious that *new* laminæ will be deposited over those

which originally belonged to the *old system*. This is why "interstitial laminæ" are always seen between the Haversian systems in a section of the compact tissue of bone, and we are indebted to Messrs. Tomes and De Morgan for their very clear and satisfactory explanation of this most important fact.

Of form, structure, and chemical composition.—The form and the structure of this and other tissues, and the chemical composition of the substances of which they consist, do not result from any fortuitous coalescence of particles, nor can it be explained by saying that, under such and such conditions, matter *must* so arrange itself, because the so-called "conditions" are present. But these so-called "conditions" are themselves but the result of a condition of things which existed previously, and so we may proceed backwards until the structure under our consideration was represented by a little granular matter, exhibiting neither peculiar form nor structure, and having a composition very different to that of the tissue it is to form.

Now, why does it form? We may answer, that in "*formation*" living particles die under certain conditions, and it is clear that the materials formed depend partly upon the conditions under which death takes place, and partly upon the relations which the elements were constrained to bear to each other just before the change occurred. Next we ask, what determined the definite relation of the elements just prior to their union to form definite structure possessing a definite chemical composition? To this we are unable to give a satisfactory answer. We

have gone back and back until we are obliged to confess our inability to explain the changes we observe. All we can say is, that the elements seem constrained to take up certain relations in obedience to some peculiar force or power (vital power). The matter of which "germinal matter" is, in all cases, composed, is for a time under the influence of vital power, while the formed material is not "living," and is the seat of physical and chemical changes alone.

Of the periosteum and so-called medullary membrane.—The periosteum is usually described as a fibrous membrane. Its outer layers exhibit simply a fibrous structure, but its deeper portion, which is continuous with the bone tissue, exhibits a totally different anatomical arrangement. Here are seen a number of elementary parts of unossified bone tissue, each consisting of an oval mass of germinal matter, surrounded by a granular-looking formed material. The periosteum is freely supplied with bloodvessels, and nerves are distributed to it. The substance or rather the deeper layer of the periosteum of a young animal is the seat of the formation not only of new bone but of complete Haversian systems. The elementary parts multiply and gradually enclose the capillary vessels in bone tissue, which at length undergoes ossification. This process has been fully described by Messrs. Tomes and De Morgan.

The medullary membrane is a highly vascular membrane resembling periosteum, but it is more delicate and contains less fibrous tissue. The vessels from both periosteum and medullary membrane pass into the openings of Haversian canals, and when these membranes are gently

torn away from recent bone the small vessels may be seen without difficulty.

Of the medulla or marrow of bone.—The medulla, as stated in a former lecture, is a form of adipose tissue, but the interesting question is, how is it formed? It exists in the cancelli, in the medullary cavity, and even in the Haversian canals. There is no doubt that the elementary parts which form at length the fat cells of the marrow, are direct descendants from the same elementary parts as those which gave origin to the cells converted into bone. The proper marrow cells (myeloid cells) may become converted into bone tissue or into marrow. During development, as would be supposed, these myeloid cells contain little or no fat, but as the bone attains its full development, many of the cells become fat cells instead of being converted into bone tissue. In the majority of birds these cells do not form fat, but as the bones are freely penetrated by air, the matter which would be fat under other circumstances, is probably oxidised and passes off as carbonic acid.

Of the development of bone.—In mammalia bone commences to form at an early period of intra-uterine life in two ways: 1. By the ossification of fibrous membrane. 2. By the ossification of temporary cartilage.

Most of the bones of vertebrata are represented, in the first instance, by cartilage. This cartilage exhibits the form the bone is to assume, but it contains no medullary cavity. It gradually undergoes conversion into a temporary and imperfect kind of osseous tissue. This is afterwards destroyed, and true bone formed in its stead. These

changes occur in all cases in which the bone is represented in the first instance by temporary cartilage in mammalia, but in the frog the cartilage becomes gradually converted into fully-formed permanent bone, and in many of the lower vertebrata the bones continue to grow during a considerable period of life, and the formation of the perfect bone results from gradual and uninterrupted changes occurring in the cartilage, new cartilage being formed as the bone increases.

The formation of the *permanent bone* in mammalia corresponds in all essential and important particulars to the formation of bone in fibrous membrane, which is not represented by any form of cartilaginous structure in the first instance.

Of ossification in fibrous membrane.—Now, the bones of man, which are not preceded by temporary cartilage, which in its turn is converted into a soft spongy form of bone, are the flat extended portions of the cranial bones; for instance, the parietal, frontal, expanded portion of temporal and occipital.

The only bones and parts of bones of the cranium existing originally as cartilage, are the base of the occipital, the sphenoid, except the external pterygoid plate, the mastoid and petrous portions of the temporal, the ethmoid, the inferior turbinated bones, the ossicles of the ear, and the hyoid bone.

The flat bones at first appear to be composed of a form of tissue closely allied to fibrous tissue. This membranous structure grows at the edges, just as the cartilage increases at the edges of the cranial bones of the frog.

Thus the gradual increase in the size of the flat cranial bones is provided for. The first deposition of the calcareous matter takes place in the central part, which is clearly that portion of the membranous tissue which was first formed. This is called the *centre of ossification*, and from this centre the process gradually extends towards the circumference. The deposition of the calcareous particles in the matrix between the masses of germinal matter, their gradual encroachment upon these, the formation of the so-called canaliculi and lacunæ has been fully discussed; nor do the changes which occur differ in their nature from those which may be observed in the process of ossification, as it occurs in some of the fibrous tissues, in old age, or in certain morbid growths. The process of formation of lacunæ may in fact be more easily investigated as it proceeds during the ossification of the fibrous walls of certain cysts, than in the formation of normal bone.

Ossification in temporary cartilage.—The temporary cartilage of the fœtus undergoes most important changes prior to the deposition of the calcareous matter in the matrix. The cells near the spot where ossification is proceeding are seen to be arranged in lines, and those close to the ossifying surface are much larger than the more recently formed cells in advance of them. It is probable that the matrix becomes more readily permeable to nutrient matter, and hence the cells increase in size. The vessels advance close to the seat of these changes, and it is possible that the passage of the nutrient pabulum in linear streams parallel to the long axis of the bone from the vessels, as from a base, may determine the linear arrange-

ment and the enlargement of the cells. Moreover, as the calcareous matter must have been carried in a state of solution to the matrix, where it is precipitated, it is obvious that at the point where the cells are the largest, much fluid has been set free, and it is probable that this may in part be taken up by these cells.

Temporary cartilage contains many vascular canals, and the *youngest* cartilage cells are nearest to these. The rate of growth of the cartilage cells and the formation of matrix gradually diminishes as we pass from the canals. The vascularity of the bone is far greater than that of the cartilage, and thus the greater supply of pabulum and the more rapid change at the ossifying surface are explained.

The calcareous matter is mainly deposited in the matrix between the lines of cells, so that a network of brittle spongy bony matter is formed. In these crypts or spaces the cartilage cells remain, and their nuclei still retain their vitality. Calcareous particles are also deposited in the material of which the outer part of the cell is composed.

It has been said that the nucleus becomes stellate, and that by the shooting out of these processes the canaliculi are formed, but this strange view has evidently been accepted without proper consideration. It would be quite as unreasonable to assert that the stellate form assumed by a blood corpuscle after its removal indicated a tendency in it to "shoot out" tubular processes, which would gradually extend and communicate with the processes of neighbouring cells.

Of the growth of a long bone in length and circumference.— The long bones grow in length by the formation of new cartilage cells at the point where the shaft (diaphysis) joins the "*epiphysis*," and each "*epiphysis*" increases in all directions by the formation of new cells at every part of its circumference, and by the slower multiplication of those already formed. The central part of the shaft (diaphysis) of a growing long bone, midway between the growing extremities, is clearly the part which was first formed, or the oldest portion of the shaft. The oldest part of an epiphysis must be the centre. In these earliest developed portions of the cartilage, bone is first formed (points of ossification). When the increase of the bone ceases after puberty, the epiphyses become connected with the shaft, and are then termed apophyses.

The temporary bone produced as above described is soon removed in order to make way for the more permanent structure, and this seems to be produced by the changes already considered which occur beneath the periosteum.

As the bone grows in circumference it is clear that all this spongy bone must be got rid of, for the medullary cavity with its marrow is about to be formed in the very spot where their temporary structure exists. The formation of Haversian systems and the exact position of the vessels is determined by the changes proceeding beneath the periosteum.

But, you will ask, what becomes of the nuclei of the original cartilage cells during and after the formation of the temporary bone in the fœtal cartilage? That they

remain active while the disintegration of the temporary bone is proceeding, I have most conclusively demonstrated, and in all probability they afterwards multiply and produce formed matter, which may in its turn undergo ossification. They also give rise to the formation of "myeloid cells," some of which take part in the formation of cancelli, while others degenerate and only produce the marrow fat cells.

It will no doubt have occurred to the reader to ask if *every* cell in the temporary cartilage and in the ossifying fibrous matrix is represented by a lacuna in the perfect bone? From what I have seen I think it probable that, as a general rule, this is the case; but it is quite possible as in cartilage, in tendon, and in muscular fibre, that some of the "nuclei" situated at the greatest distance from the nutrient surface may gradually undergo transformation into the formed material, as I have described in the case of permanent cartilage, with the exception of a very small portion of germinal matter which dies and leaves a small space occupied with fluid. Such "cells" would, therefore, be obliterated, and would not be represented by lacunæ.

Of the germinal or living matter of bone—Of caries and necrosis.—In the development of bone, in the removal of old Haversian systems, and in the formation of new ones, in the union of fractured ends of bones, in caries and in the formation of bone cancer, "cells," or rather masses of germinal matter are the active agents. If bone is to be *absorbed* these little masses of germinal matter multiply very rapidly and increase at the expense of the surround-

ing bone. On the other hand, if bone is to be *formed*, the masses of germinal matter, having increased in number for a time, cease to multiply, but each increases in size, and the outer part of each slowly undergoes conversion into formed material, which in its turn becomes gradually impregnated with hard calcareous salts. The harder the bone is to be, the slower must this process proceed.

In rickets, caries, and cancer, the vital changes going on in osseous tissue are too active. Increase is proceeding too fast, for the condensation of the tissue which is produced, to take place. Here, as in all other cases, rapid change is associated with brief duration, while the well-developed normal lasting tissue is formed very slowly, and the changes succeed each other in the most gradual, orderly, and regular manner.

In caries, the germinal matter of a part of a bone receives too large a supply of nutrient matter, it grows too fast, and lives upon the surrounding tissue which has been already formed.

In necrosis, the death of the germinal matter of many lacunæ takes place. It is easy to conceive that such a result must ensue if the supply of blood be cut off, for the currents of fluid, which during life permeate every part of the bone, cease, and the entire mass which has been affected by these changes must die.

Changes in the small trunks which supply the Haversian vessels, ending either in their obstruction, as, for example, by clots, or in their obliteration by pressure exerted upon them, as from the growth of adventitious tissue around, may cause necrosis of a considerable extent of osseous

tissue. Thus effusion into the deeper and more spongy portion of the periosteum, as occurs in the formation of a node, may cause the occlusion of some of the vessels passing from this membrane into the compact tissue. The passage of blood through these vessels being interfered with, the germinal matter of all that portion of bone receiving nutriment from them must die, and a piece of bone of considerable size may become "necrosed." Immediately around this the nutrient matter would flow more freely, but of course less regularly. In consequence the germinal matter of the neighbouring lacunæ would grow much faster, and thus a number of granular cells would result. These would even eat away, as it were, but of course very slowly, the dead bone, which soon becomes surrounded with such cells. After these have accumulated to a certain extent, many increase in size, produce formed material, which in its turn ossifies, and thus the piece of dead bone becomes surrounded, and at length embedded in new irregularly formed bone. This process goes on, unless the whole of the dead bone (sequestrum) is removed by the process above referred to, or by surgical interference. Before the dead bone can be removed by the surgeon, he has to cut away very much of the new bone which has been produced.

Now, it has been said that the dead bone acts as an irritant—as a foreign body—and that this is why the bone increases around it, and this view is still strongly maintained, although no one has been able to show exactly what is meant by the supposed "irritation." It has been assumed that an irritant or excitant is always neces-

sary to increased action, that by this "irritant" the living cells are "excited" to live faster than usual. But I have shown that for this increased activity all that is required is a more free access of nutrient matter. The so-called "irritant," instead of "exciting," acts in the most passive manner possible. It allows pabulum to have freer access to the living or germinal matter. It removes to some extent the restrictions under which growth normally takes place. There is no "excitation to increased action" at all. The more freely living matter is supplied with pabulum the faster it grows. "Increased action" in a living structure results from the *removal of restrictions*, as occurs in the *rupture*, *perforation*, or *softening* of the "cell wall" or "intercellular substance," when, of course, the nutrient pabulum comes more readily into contact with the germinal matter, *not from "stimulation," "excitation," or "irritation."*

LECTURE IX.

TEETH.

On teeth—The dental tissues not disintegrated and renovated—Of the dental tissues—The development and formation of teeth—The structure and formation of the dentine—Of the pulp of the tooth—The structure and formation of the enamel—The structure and formation of the cementum or crusta petrosa—Of the nature of the teeth—Are teeth entirely epidermic, or in part dermic and partly epidermic, or are they entirely epidermic structures?—Are the dental tissues allied to epithelial or connective tissues?—Of the membrana prœformativa—Of the homology of the dentine enamel and cementum—Of the formation of the so-called intercellular substance of dentine—Of the development and formation of the palatine teeth of the newt, which are formed entirely from epithelial structure—The relation of the tooth sac to the proper dental tissues—Summary of the different views now entertained upon the development of teeth—Of caries.

Gentlemen,—Although I am unable to give a clear or complete account of the changes occurring during the formation of a tooth, I shall have no difficulty in convincing you that the study of these dental tissues is of the utmost interest and importance, not only to those who are to devote themselves specially to dental practice, but to every student of physiology and medicine.

We shall necessarily be led to discuss most important questions connected with Formation, Nutrition, and Growth, and the anatomy of the tooth structures is of special interest to me, because the changes I shall have to

describe receive, I think, a most satisfactory explanation upon the new views I have propounded in this course of lectures.

You will find that, as in the case of bone, many authors, in describing the anatomy of tooth structure, have described, not the living growing tissue, but dead and dried texture. In dentine, tubes or canals containing air have resulted from the drying up of the soft matter which occupied them during life, and to these *artificial* channels the office of transmitting nutrient fluid to every part of the tissue has been assigned, but, as it seems to me, upon most insufficient grounds.

The dental tissues not disintegrated and renovated.— These dental tissues of all the textures in the body are those which undergo the least amount of change, and the statement that the material of which our teeth are composed is being continually removed and renewed, is a mere assertion, and utterly unsupported by facts or by sound argument.

It has often been asserted that *all tissues* in the organism undergo constant change during life; but this statement is only in part true. Nevertheless, observers have, one after the other, received it in its widest signification, and, accepting the dictum as true, have allowed inferences derived from actual observation to be modified by it. Thus it has been asserted that both bone and teeth have a system of tubes through which *new particles* are carried to all parts of the structure to replace the *old ones* which are removed by the same channels. But I will assert the very contrary, and I am sure no one will contradict me when I

say that the very particles of calcareous matter which exist now in the enamel and dentine of our teeth will be there until they are destroyed by disease, worn away by friction, or removed bodily by extraction. It cannot be too distinctly stated that there are tissues in the body which are so slowly changed that it is not possible to demonstrate that they change at all, save in undergoing some degree of condensation after their formation, and there is matter which seems to be destroyed as fast as it is produced—probably so very fast that we cannot even obtain for examination, the matter itself, but only the substances which result from its decomposition. Between these two extremes there are tissues which exhibit very different rates of change. There is no evidence of addition and removal of material going on in the enamel and dentine after the completion of their formation, and it is probable that the matter upon which the hardness of these tissues depends is not removed at all after its deposition.

Of the dental tissues.—The structures of which the human teeth are composed are three in number—1, dentine or tooth bone; 2, enamel; 3, cementum or crusta petrosa. Of these the two first are the most important. The third exists as a thin layer over the fang of the tooth.

The enamel is the hardest of the three structures. The dentine is the next in hardness, and the cementum is the softest of the dental tissues.

At an early period of development all these tissues were quite soft. Their hardness, like that of bone, is due entirely to the deposition of calcareous salts in the soft tissue. The formation of soft matrix in the case of the

dentine, and its impregnation with calcareous matter continues to take place even in the adult, for there exists in the dentine a cavity which is occupied in the recent state by a soft and very highly vascular structure in which nerves are very freely distributed. This is called the "*Pulp.*" Upon the surface of this pulp the formation of dentine continues to go on. As age advances, the pulp shrinks and the pulp cavity becomes smaller, but the pulp *is not itself converted into dentine*, as some have taught.

The greater part of the tooth is composed of dentine, and this may be regarded as the most important as well as the most constant of the dental tissues.

The development and formation of teeth.—At about the sixth week of intra-uterine life little papillæ may be seen rising from the mucous membrane of the dental groove. Each papilla is said to consist of the epithelium and subbasement tissue, with its vessels and nerves. The mucous membrane around each papilla is described as rising up and gradually enclosing it in a sort of follicle. The lips of the follicle rise higher, and at last reach above the summit of the papilla and close over it. The papilla thus becomes enclosed in a capsule. From the side of this follicle, before it is completely closed up, a portion is, as it were, pinched off, so that a second cavity is gradually formed by the side of the larger one, and at the bottom of this second sac or cavity another papilla makes its appearance and undergoes similar changes. This is the papilla which at length becomes the permanent tooth. My own conclusions differ in some essential particulars from the above views of Professor Goodsir, which are generally accepted

and taught; but I will defer stating the differences until the anatomy of the dental tissues has been described.

The formation and structure of the dentine.—Even by the fourth month of intra-uterine life the formation of the dentine has commenced quite at the summit of the papilla. This thin shell of dentine does not change, nor is it altered, but it remains as the summit of the dentine when the tooth is fully formed. As it extends gradually at the circumference the whole papilla increases in size, so that by the time a thin shell has been formed corresponding to the surface of the crown of the tooth, the pulp corresponding to this has already attained its full size. Across the fully-formed dentine, near the summit, lines may be observed which mark the different diameter of the pulp, and the varying degree of convexity of the upper surface as the formation of the tooth progresses.

It must be distinctly borne in mind that the dentine grows constantly in one direction only, from without inwards, and therefore, when the extreme *circumference* is once formed, it is not possible that the tooth can increase in diameter by dentine, since dentine is never normally formed upon its outer surface. These processes continue, and the tooth gradually increases in depth by the formation of the fang which projects downwards towards the socket which is being formed for its reception.

The actual tissue which becomes the dentine differs materially from that of which the great body of the papilla is composed. Before any dentine is formed, and immediately beneath the dentine last formed at all ages—between it and the vascular and nervous pulp—is a layer of what

looks something like nucleated columnar epithelium. This tissue consists of elongated cylindrical bodies, or cells with "nuclei," which are placed at right angles to the outer surface of the pulp. Although the pulp diminishes in size while the formation of the dentine proceeds, the pulp does not become the dentine. Nor is the dentine formed by the *deposit* of calcareous matter *beneath the "basement membrane,"* as has been asserted by Prof. Huxley; but this dentine results from changes occurring in a tissue which lies upon the surface of the pulp. This consists of cells like columnar cells. These elongated cells are not separated from the nerves, vessels, and connective tissue of the pulp by a demonstrable basement membrane, but their extremities pass amongst the fibres of the connective tissue, and in some instances seem to be continuous with them. The relation seems similar to that which exists between the epithelial cells in contact with and adhering to the tissue of a papilla of skin, or of the tongue, or of the mucous membrane of the fauces, and as in these cases prolongations from the cells seem to pass amongst the fibres of the connective tissue. It is possible that some may be continuous with the so-called connective tissue corpuscles. As new dentine is formed, these cells encroach upon the pulp, the constituent tissues of which gradually diminish in amount.

The changes taking place in the calcification of the organic matrix, after it has been formed by the cells, can be studied quite as satisfactorily in a fully formed as in an embryo tooth. The changes occurring during the formation of the dentine as it proceeds in the adult tooth are,

indeed, of the same nature as those which take place during the development of this tissue in the embryo.

There are few anatomical questions which have given rise to more controversy, than the structure and mode of formation of the dentine, and the very last writer on the subject, M. Lent, describes the dentinal canals as consisting of direct processes of the whole dentinal cells. "The matrix of the dentine is not formed of the dentine cells, but is a secretion of these cells and of the tooth pulp—in other words, an intercellular substance."* Now, Mr. Tomes has shown that the "dentinal tubes" are occupied with a soft solid structure which may be seen projecting in the form of solid processes from the broken ends of the dentinal tubes. The truth of these observations has, however, been doubted by several observers. I have been able to verify Mr. Tomes' statements as to the dentinal tubes being occupied with this soft structure, and now pass round a preparation in which this material has been coloured red with carmine, and is most clearly demonstrated. The dentinal "tubes" of a *living tooth* are never empty; indeed, they are not tubes, nor are they canals for the transmission of nutrient substances dissolved in fluid, but they contain as already stated a soft solid substance, a portion of which, near to the pulp, is in a state of active vitality.

Imagine for a moment one of the "soft nuclear" fibres of tendon surrounded with a matrix impregnated with calcareous matter, and you will form, I believe, a good

* Kölliker's Manual of Microscopic Anatomy, p. 307.

idea of the structure of the "dentinal tube" and its contents.

The wall of the tube with the matter between the tubes corresponds to the "wall" of an ordinary cell, or to this and the intercellular substance (my *formed material)*, and the central part of the contents of the tube to the granular cell contents with the nuclei (my *germinal matter).* If you look at the tissue of the pulp just beneath the surface of the dentine you find a number of oval masses of germinal matter coloured intensely red by carmine. These are nearly equidistant and separated from one another by a certain quantity of material which is only very faintly coloured, and in cases where the solution was not very strong it remained colourless. This colourless matrix is continuous with the *intertubular dentinal tissue*, while the intensely red germinal matter, or rather a prolongation from it, extends into the dentinal tubes. The germinal matter with a thin layer of soft and imperfectly developed formed material is easily detached from the more condensed formed material around it, and thus its continuity with the dentinal tubes may be destroyed. The whole then appears as an oval mass (cell) with a prolongation or process which occupied the dentinal tube.

The general description given of the manner in which these dentinal tubes *open* upon the walls of the pulp cavity is certainly true, but it is true only of the dry tooth. In the living tooth a prolongation from one of the "cells" on the surface of the pulp is prolonged into each tube. The tubes cannot, therefore, serve as mere conduits for nutrient fluids which transude through the walls of the vessels, and

are supposed to pass along the tubes to the outer part of the tooth. Moreover, in some cases certain of the so-called dentinal tubes become completely solidified, the tube being obliterated. These points receive a ready explanation from a careful consideration of the facts I have brought forward.

The specimens which I have shown prove, I think, that the formation of the dentine and the so-called tubes, is effected in a much more simple manner than is usually believed. The elongated masses of germinal matter first of all produce *formed material*, which gradually increases as in other cases, upon the outer surfaces of the germinal matter. The formed material of the adjacent elementary parts is continuous, and calcareous matter is first deposited in the oldest part of this formed material. The calcareous matter appears in the form of small globules, which gradually increase in size, and often several coalesce. Thus the formed material, or matrix of the dentine, becomes calcified.

Not unfrequently, however, several of the calcareous globules increase in such a way as to enclose a portion of uncalcified matrix. This being, as it were, imprisoned by hard impermeable structure, retains its soft primitive state. If the tooth be dried the soft matrix in these spaces shrinks and air rushes in. Thus the appearance known as "globular dentine" is produced, and the reason why uncalcified tubes are seen traversing these spaces becomes manifest; as in the formation of bone already described, spaces or pores are left through which nutrient matter passes towards the germinal matter. In this way very fine

channels result, which may be seen in the dry tooth passing from one dentinal tube to the other.

After the "matrix" of the dentine is calcified, the germinal matter still slowly undergoes conversion into more formed material, which in its turn becomes impregnated with calcareous matter. The germinal matter diminishes in thickness. The formed material is produced more slowly after the general basis has been laid down, and hence the dentine immediately surrounding the tube seems to be distinct from that lying in the intervals between the tubes. It is probable that the difference in compactness and hardness results merely from the so-called "matrix" which was first produced, having been formed more quickly than the so-called wall of the dentinal tube.

The germinal matter which takes part in the formation of the matrix gradually becomes changed into dentine, from the outer part of the dentine (the oldest portion) towards the pulp-cavity, where these changes still go on. In the dry tooth the same fact may be expressed by saying, that the *narrowest part* of the dentinal tubes is at the *circumference* of the dentine, and this part was the first formed; *the widest* part is that which is *in contact with the pulp*, and this is composed of dentine most recently developed. Internal to this is a narrow layer, the formed material of which is not yet calcified.

The varying diameter of the tubes in different parts of the dentine may be seen in sections, and the facts demonstrated are confirmatory of the views offered.

The appearances I have described can only be demonstrated in perfectly fresh teeth, which have been placed

in carmine solution very soon after extraction. The principal changes in such a tissue as dentine seem to consist of the conversion of germinal matter into formed material, and the impregnation of this formed material with calcareous matter, rapidly at first, but more slowly as the quantity of calcareous matter increases. In the adult, the remains of the germinal matter slowly undergoes conversion into formed material, and this slowly becomes impregnated with calcareous cells. In old age, although the pulp is very much reduced, this conversion is not complete, and a certain amount of germinal matter still remains in the tubes and in the pulp cavity from which dentine might have been produced.

Of the pulp.—The *tissue* of the pulp, it must be distinctly borne in mind, is not converted into dentine; neither does dentine, nor the tissue from which it is formed, exhibit any characters which justify our classifying it with the connective tissues. It is not, however, formed independently of any of the histological elements of the pulp, as asserted by Huxley, for no dentine was ever produced except by the agency of the so-called "cells" above referred to (see figs. 57, 63, and 64 in "The Structure of the Simple Tissues"). I agree with Kölliker and Lent that the dentinal cells are the only active agents concerned in the formation of the dentine, but cannot regard the canals as direct processes of the whole dentinal cells, nor admit that the matrix is an intercellular substance, the "*secretion of these cells and of the tooth pulp*," as they maintain. I have advanced already many facts against the general views regarding this so-called intercellular substance, which I need not repeat here.

The assertion that the matrix is a secretion from the cells and the tooth pulp, accords with the dictum that the intercellular substance of cartilage and bone arises *partly* as a secretion from the cells, and *partly* from the blood independently of them (Kölliker). Such statements can scarcely be considered as hypotheses. They are mere authoritative assertions, in support of which no facts are given or arguments advanced.

As the tooth advances in age the pulp becomes smaller. The relation of the nerves and vessels to the youngest dentine always remaining the same. The nerves may be seen in vast number, forming bundles, composed of numerous large dark-bordered fibres, which interlace freely with each other, and divide near the surface of the pulp into bundles, composed of fibres, which become finer and finer. The ultimate fibres with their oval nuclei are very freely distributed upon the surface of the pulp just beneath the large oval nuclei or cells, which take part in the formation of the dentine, and the fibres run among the prolongations of these cells. The nerves and vessels pass in a direction at right angles to the dentinal cells and tubes. The mass of the pulp is composed of a simple form of connective tissue, with numerous oval and triangular corpuscles (germinal matter), not unlike that of which the mucous tissue of the umbilical cord consists. There are no true fibres of yellow elastic tissue, but many of the fine nerve fibres which run in bundles of white fibrous tissue might easily be mistaken for them. In many old teeth the pulp cavity is almost obliterated.

Of the formation and structure of the enamel.—Great dif-

ference exists among observers with regard to the formation of enamel. It is said that after the tooth sac has completely closed a change takes place upon its inner surface, and a quantity of a very peculiar form of connective tissue is produced. It seems to consist of stellate cells, almost like those composing the pith of the rush, a form of vegetable tissue termed *actinenchyma*. This tissue has been well described and figured by Todd and Bowman, who regard it as composed of a web of fibres, the meshes of which contain a clear fluid ("Physiology of Man," vol. ii.) It has, however, been clearly shown by Huxley that the actinenchymatous tissue of the calf's tooth does not correspond to the stellate tissue of man. The first is a modified sub-mucous connective tissue, while the last is an altered epithelial structure. This peculiar tissue has been considered by John Hunter and by the majority of observers since his time, as an organ concerned in the formation of enamel (enamel-organ). Upon its inner surface is a layer of elongated cylindrical cells, arranged precisely as columnar epithelium. These cells constitute the so-called enamel membrane, and it has been generally believed that in the formation of enamel the cells become calcified, and that, in fact, the prisms of enamel are nothing more than the calcified cells of the enamel organ. If this be true, it almost follows that the enamel corresponds in its position and structure to the epithelium of a mucous membrane, while the dentine must be regarded as a modification of the sub-basement tissue, and the position of the basement membrane would be between the enamel and the dentine.

It is, however, quite certain that the pulp is not more directly concerned with the formation of the dentine than the enamel pulp is with the formation of enamel. Both dentine and enamel are formed from elongated nucleated bodies which have been spoken of as cells. These cells, which form the matrix of the dentine, as has been shown, gradually move inwards, while the pulp diminishes in proportion. The power of change resides in the germinal or living matter of the cell itself, not in the membrane above or below it, or in any other matter.

Professor Huxley, however, asserts that the enamel is not produced by any conversion of a cellular structure. "The fibres of which it is composed are structureless and almost horny." Its existence and its structure are to be considered as ultimate facts not explicable by the cell theory.* Mr. Huxley's view has not been confirmed by Mr. Tomes ("Dental Surgery," pp. 265, 270), and I have had no difficulty in demonstrating elongated bodies, each having a distinct nucleus, the portion nearest the dentine being calcified while the greater part still remains granular. I have some specimens preserved in which the whole process can be demonstrated. These bodies are as much "cells" as epithelial particles are "cells."

Professor Huxley maintains that all the dentinal tissues are *dermic* and not *epidermic*. By the action of acetic acid he raises a membranous structure from the outer surface of the enamel, and, moreover, asserts that the cells of

* "On the Development of the Teeth," &c. *Quarterly Journal of Microscopical Science*, vol. i., page 149. 1853.

the so-called enamel membrane are not directly concerned in the formation of enamel, but that the enamel rods are produced *beneath* it.

The "membrane" thus raised by the action of acetic acid really consists of the altered outer uncalcified part of the columnar cells already described, and the "enamel rods" seen "beneath" it, are really the *calcified portions of these very same cells.* Mr. Tomes has, in fact, shown that this so-called "membrane" is to be split up into columns, and rightly maintains that it cannot therefore be a "*membrana præformativa*," as it is considered by Huxley.

The outer extremities of the prismatic calcifying cells of the enamel are of course composed of soft material. It is this superficial uncalcified portion which may be torn away from the deeper and calcified portion in the form of an expanded membrane. By the action of acids it swells up and becomes transparent, and seems to be a membrane covering the enamel rods. Mr. Nasmyth was the first to draw attention to the existence of such a membrane, which was to be demonstrated by the action of an acid, covering the enamel even when fully formed, but before it had suffered from friction. This was considered by him to be the persistent dental capsule; but Mr. Tomes has shown that this, Nasmyth's membrane, is continuous with the cementum of the fang of the tooth, and is rather of the nature of uncalcified cementum than præformative membrane.

The elongated cells which become calcified to form the enamel rods or prisms are, however, situated entirely beneath a thin membrane, to the under surface of which the most superficial portion or summit of these cells adheres.

This membrane is highly vascular, and I have succeeded in making beautiful injections of it in the canine tooth of a young pig about three months old. In the same specimen there are numerous enamel cells which are calcified in the lower part near the dentine, while the more superficial portion remains granular and still contains a very large nucleus. The enamel cell increases in length as the so-called nucleus moves away in a direction *from* the dentine. The calcareous matter is deposited first in that part of the "cell" which is nearest to the dentine, and which was first formed, and it is deposited as small columnar masses in successive layers, which are indicated by transverse lines in the fully-formed enamel rods.

Of the structure and formation of the cementum or crusta petrosa.—The cementum is often stated to be true osseous tissue, but it differs from bone in many important particulars. The lacunæ which it contains are often very much larger than those in bone, and they are most irregularly arranged. The "matrix" of the cementum is more transparent and harder than that of bone, and much of it consists of a very clear transparent structure of a refractive power and hardness much resembling dentine, with small tubes traversing it here and there, but their arrangement is most irregular. Thin layers of cementum, it is well known, are destitute of lacunæ, but I have specimens even of the 1-100th of an inch in thickness in which not a lacuna is to be seen, and even in cementum much thicker than this very few lacunal spaces are sometimes to be found. The canaliculi are often of great length, and many are seen to extend almost in a right line

from a space in the substance of the cementum quite to its surface. Nutrient fluid must be almost entirely derived from the outer surface of the cementum, and hence these channels remain as the tissue increases in thickness until the mass of germinal matter in the lacuna dies, and they are often of great length.

It is generally stated that the cementum results from the ossification of the tooth sac, but, as remarked by Kölliker, cells take part in the formation of this tissue as in the formation of bone, and the tooth sac is not transformed into cement. The cement is continuous with the dentine, and, as observed by Tomes, the dentinal tubes may often be traced into the structure. Cementum is formed much more slowly than bone.

If the fang of an adult tooth properly prepared be examined, a very beautiful soft tissue will be found upon the surface. This takes part in the formation of the cementum, and is concerned in the formation of those exostoses which often grow upon the fangs of the teeth.

It is composed entirely of what may be described as branching cells (elementary parts), the processes of which anastomose freely with each other. It is from this tissue that the crusta petrosa is formed. It is a most perfect example of a tissue consisting entirely of cells, the cavities of which *communicate with each other by tubes.* The stellate cells are here as distinct as they are in the pith of the rush. But do these cells and tubes merely constitute an elaborate system of channels for the distribution of nutrient material to the tissue which intervenes between them, as Virchow and his school maintain? This tissue, it may be remarked,

grows very slowly; it is a very low simple form of tissue, and probably requires but very little nutrient matter. If the above view is adopted it must be admitted that the means for nourishing the structure are far more elaborate than would be expected, supposing the conclusion is accepted that there ought to be a constant relation between the activity of change in a tissue and the mechanism for bringing new matter to the elementary parts and carrying off the effete material from them.

Neither does it appear that all these bodies become lacunæ of the cementum. The stellate cells just described for the most part have not more than from ten to twelve processes or tubes projecting from them, while many of the lacunæ of the cementum have as many as thirty or forty, hence these tubes are certainly not an early stage of the canaliculi, and the cells cannot become lacunæ simply by the deposition of calcareous matter in the intervening matrix or intercellular substance.

This stellate tissue on the surface of the fang nevertheless undergoes calcification. The processes of the stellate masses become narrower and narrower until the germinal matter which they contained, having undergone conversion into formed material, they cease to be coloured by carmine. They now look like roundish, highly refracting cords, which are colourless, and connect the several stellate masses of dark-red germinal matter with each other. Here and there in the intervals between these processes small globules of calcareous matter have been deposited, and these increase and completely surround the cord-like processes. Many of the processes gradually assume the character of the sur-

rounding matrix, disappear as distinct cords, and like the rest of the tissue become impregnated with calcareous matter. It is in this manner that the tissue of the cementum, which exhibits a laminated arrangement, but is destitute of lacunæ, is produced.

Many of the stellate masses of germinal matter (cells) shrink and disappear in consequence of the same changes having occurred. Others remain with their processes, and their nuclei possibly remain as the nuclei of the lacunæ which are irregularly distributed through the cementum; but I cannot express myself positively on this point. It is certain that all the cells do not become lacunæ, for in this tissue there are half a dozen stellate cells to one lacuna in the cementum, and many of the canaliculi are five times as long as these tubes. Are these processes tubes? This question would doubtless be answered in affirmative by every one who examined the tissue long after death; but during life they contain a solid or semi-solid substance corresponding to that which occupies the so-called dentinal tubes. They contain portions of the germinal matter which is undergoing conversion into formed material, and the situations in which these "tubes" existed are the last portions of the formed material to undergo calcification.

This is precisely the same change which takes place in the calcification of the dentine, the only difference being in the form which the masses of germinal matter assume in the first instance. Cementum is a more permanent but less perfect tissue than bone.

On the nature of teeth and of the tooth structures.—It is impossible for any one who has studied anatomy, even in

the most superficial manner, not to feel interested in Homology. Every student delights in tracing out the different organs in the several classes which correspond in essential structure and mode of development, or are homologically related to one another; so one of the highest aims of the minute anatomist is to define the particular elementary structures or components of the different textures which correspond.

The homological relations of the teeth as organs, or of the dental tissues, have not yet been positively determined, and several different views have been taught and are entertained by high authorities upon this very difficult subject.

Teeth have been considered to be part of the skeleton. Many think they are closely allied to bone.

Teeth have been regarded as papillæ, the enamel corresponding to the epithelium. The dentine and pulp to the papilla itself. According to this view the enamel lies external to the basement membrane, and the dentine answers to the submucous tissue. A certain general agreement in arrangement and mode of growth has been admitted to exist between teeth and hairs. Prof. Huxley admits that teeth are homologous with hairs; but he thinks that both these organs are dermic, and not in any part epidermic. He thinks that *all* the dentinal tissues are produced beneath a membrana præformativa, and considers that the enamel is developed not *upon* but *beneath* basement membrane. He thinks that scales and feathers may come into the same category, but would admit nails to be purely *epidermic*.

Although upon a question so very difficult of investiga-

tion and so complex in its bearings, I hesitate to express too positive an opinion, it is right that I should direct your attention to the different doctrines that are taught, and try to show which view receives the strongest support from a careful consideration of facts that may be demonstrated. I regret that the conclusions to which I have been led differ in several important particulars from those held by many authorities on this matter.

Are the tissues of the teeth allied to epithelial or connective tissues?—The first question we have to discuss is to what textures the tooth tissues are most nearly allied. A tooth has often been compared to bone, and it has been said that the pulp cavity corresponds to the Haversian canal, and the comparison has been made still more precisely. It has been said that just as we find a vessel in the Haversian canal, so we find vessels in the pulp cavity, and just as we have the canaliculi opening upon the walls of the Haversian canal, we have the dentinal tubes opening upon the vascular surface of the pulp. The fluid nutrient plasma passes along the canaliculi of the bone, and thus every part is nourished, and in dentine the tubules are the channels by which nutrient matter is distributed to the hard dentinal tissue.

Let us consider if the tooth is more closely allied to the *antler*, which is composed of bone, or to the *horn*, which, as is well known, is but a modified cuticular or epithelial structure. It should be premised that there are examples of teeth which are continually being removed and replaced by new ones, which grow up behind them, or beneath the old ones,—teeth which once

removed are never replaced,—and teeth which continue to grow regularly throughout life from a persistent pulp, as it has been called. Some of these teeth are worn away as fast as they are produced, while others, as tusks, increase in length as the animal advances in age. With reference to the tusk and the horn it will be remarked that both continue to grow on from the nutrient pulp. That tissue farthest from the pulp is the oldest, that nearest to it was only recently produced. The vessels of the pulp do not penetrate into the substance of horn, or the tusk, or tooth. Moreover, the oldest part of these organs is the narrowest, and as the creature grows, the diameter of the horn and tusk which is produced increases, and if not worn away by friction the very same tissue which was formed in youth remains in old age. This oldest tissue gradually passes into that which has been lately produced. Nor is it possible, as many have supposed, that the oldest horn or tooth structure formed is replaced by new. The very same matter remains throughout life, and undergoes little further change than desiccation. Even in very old animals, both horns and tusks continue to grow slowly. There are, therefore, important points connected with their mode of growth, form, and general changes, in which tusks and horns resemble one another. We shall presently consider if they agree in their minute structure.

On the other hand, every part of the *bony antler* is penetrated by vessels. Even to its extremity the blood circulates. It grows in every part, nor is there the remarkable difference in diameter at its apex and base, as observed in the case of horns and tusks. It does not continue to

increase as the animal advances in age, but, as is well known, drops off at intervals, and is replaced by an entirely new structure. The horn of the young animal passes uninterruptedly into the horn formed in old age; but the bony antler of youth is separated from that produced in old age by many entire organs which have successively been developed, grown, reached maturity, died, and have been cast off.

If any analogy exists between the pulp cavity of the tooth and the Haversian canal of bone, it is clear that the tusk and horn correspond, not to the entire antler, but only to that small portion of bony tissue which surrounds each Haversian canal.

If the elementary parts of which the horn is composed were calcified a "tusk" would result. But neither in mode of development, nor in structure, nor in growth, nor in its persistent character, does the antler agree either with horn, hair, tusk, or tooth. So far, therefore, it would appear that the hard calcified texture of which the tusk or tooth is composed corresponds more closely with that of the epithelial or epidermic horny tissue than with osseous texture. We will now discuss the position of the basement membrane of the tooth.

Of the basement membrane, or membrana præformativa.—I propose now to refer briefly to the dispute concerning the position of the membrana præformativa. It is, however, necessary to remark, in the first place, that in no case has any such transparent membrane, as that supposed to exist, anything to do with the *formation* of the structure upon or beneath its surface. Its presence, as is well known,

is by no means constant, and with regard to its actual existence in relation to any of the dental tissues, I regard it *as certain that no præformative membrane has been actually demonstrated over the enamel, as Huxley asserts, between the enamel and dentine, as many observers hold, or beneath the dentine.* That a transparent membranous-like structure may be raised from the surface of the enamel of a young tooth by the action of chemical reagents is perfectly true, as stated by Huxley; but it has been already shown (page 163) that this is not a præformative membrane. It consists undoubtedly, as Mr. Tomes maintains, of the outer as yet uncalcified part of the columns or columnar cells, which take part in the formation of the "enamel rods." This, then, is but a *membranous appearance* produced artificially, not a natural membrane taking any active part in the formation of the enamel, or even a membrane beneath which enamel is *deposited.* I have already shown that there is a vascular membrane external to the enamel cells, but this does not hold the relation to the formed enamel tissue, which the supposed præformative membrane is said to possess.

It is certain that no basement or præformative membrane exists between the enamel and the dentine, for in many instances the latter tissue actually extends into the former, as was first shown by Mr. Tomes (Phil. Trans.)

With regard to the existence of such a structure upon the surface of the pulp—that is, beneath the enamel—I have already stated that, as in the case of the papillæ of skin, the cells seem to dip down, as it were, into the substance of the so-called sub-basement connective tissue. Still,

there can be no doubt that the position of the basement membrane, supposing it to be a necessary and constant anatomical structure, would be between the epidermis of the skin and the modified connective tissue of which the body of a cutaneous papilla is composed. Most observers seem to have concluded that a membrana præformativa was an absolute necessity, without which different structures could not be produced; but these structures, it has been clearly shown, are the result of changes occurring in a special tissue, not in the so-called membrana præformativa, which is perfectly passive. It seems to me that such a membrane has no more to do with the *formation* of structures beneath it than the capsule of a seed with the formation of the seed itself. Membranes where they do exist are the most passive of structures. Neither the dentine, nor the enamel, nor the cementum, are formed by any membrane. The active matter concerned in the formation of this, as in all other cases, is that part of so-called "cells" which I have described as "*germinal matter.*"

The homology of the dentine, enamel, and cementum.—Still the question of the situation of the basement membrane must not be thus dismissed or the real question at issue avoided. We will, therefore, proceed to the consideration of the larger question regarding the actual relation of the enamel and dentine to the tissue of which the pulp of the tooth is composed. Where, in the tooth, is the line situated at which the cellular or epidermic structure joins the dermic? Upon the determination of this question will depend the conclusion we accept as to the true homology of the dental tissues.

I have advanced facts and arguments against the view that the enamel and dentine lie *beneath* basement membrane, and are dermic structures, and I have shown that there is great improbability in the view that the dentine itself is a form of connective tissue; but this part of the question will be more carefully investigated in the next section.

It remains, then, to be considered if the dentine, like the enamel, is allied to an epithelial structure. This last is the inference, which, though widely differing from any now generally held, seems to me to receive the strongest support from a careful consideration of the whole question of the anatomy and development of the teeth.

In many epithelial structures, as is well known, the cells or elementary parts upon the surface exhibit a difference in arrangement and form, from the deeper ones, at least as remarkable as that observed between the dentine and enamel. I look upon both enamel and dentine as calcified "*epithelial structures.*"

Dentine.—The cells from which the dentine is formed exhibit some analogy to elongated epithelial cells, and there are not wanting instances where the deep extremities of epithelial cells may be traced for a considerable distance, and may even be followed in "sub-basement tissue."

In many cuticular structures great difference is observed between the cells upon the surface and those beneath, so that it would seem that the outer cells grew outwards, while the inner cells grew inwards towards the sub-basement tissue. It seems to me that in dentine and enamel

we have a somewhat similar arrangement. These two tissues grow in opposite directions from the same point. So far from both the dentine and enamel being *dermic* structures, as Prof. Huxley concludes, they are really both *epidermic*, and the enamel and dentine are both homologous with epithelium of cuticle, the first with the superficial, and the second with the deeper layer.

Epithelial structures may often be traced into connective tissue, and it is therefore not surprising that, supposing the dentinal tissue to be modified cuticle, that it should be continuous with the cementum—a structure closely allied to bone. Just as we have bone projecting outwards upon the surface, so we may have tissues, which, although formed upon the surface, extend for some distance into deep parts, and thus come into very close relation with deep structures.

The general arrangement of the dentine far more closely resembles that observed in epithelial than in bony structures. The hair grows from the surface of a pulp like the tooth. Many hairs and many teeth grow from persistent pulps. The pulp undergoes but slight change in size, although the bulk of tissue produced upon its surface is enormous. The vessels and nerves of the papilla no more penetrate to the extremity of the hair than do the corresponding structures pass towards the extremity of the tooth. There is, as has been shown, the strongest analogy between the growth of a tusk and that of a hair, and if we compare the textures of the two structures it is not possible to help noticing many points in common. It is not difficult to find in epithelial structure elongated epithelial cells applied

to each other like the anatomical elements of the dentine. Nor do the so-called dentinal tubes present any serious impediment to the acceptance of this view, for it has been positively demonstrated that they are not tubes for the circulation of nutrient fluid, but are always occupied with solid matter. Moreover, as the elementary parts of the dentine advance in age, the soft solid matter in the centre (occupying the supposed tube) gradually undergoes conversion into dentinal tissue, just as the germinal matter of an epithelial cell gradually undergoes conversion into hard tissue as the cell advances in age.

Enamel.—The cells which become the enamel, grow from within outwards, and the distance from the so-called nucleus to the deepest part of the enamel gradually increases. The germinal matter ("nucleus") gradually moves outwards, deriving its nourishment from the outer or upper surface, and producing formed material at the opposite extremity. This formed material takes the form of a prism, and its oldest portion—that is, the part nearest to the dentine—gradually becomes impregnated with calcareous matter. When the enamel thus produced has reached a certain thickness, the germinal matter, *nucleus*, dies, the tooth passes through the gum, and the vital changes occurring in the enamel cease for ever. No new enamel is formed, but that produced is gradually worn away: but in the rodent incisors, the formation of enamel like that of dentine proceeds from the persistent pulp. Nor is there any reason whatever for believing that the fully formed enamel is "nourished" or appropriates nutrient matter. Doubtless it is permeated very slowly by fluids which preserve its hardness, but these

fluids act only as similar fluids would act upon the structure if it was entirely removed from the body.

Let me again impress upon you the fact that the formation of the enamel is complete, and ceases at an early period of development, while the formation of dentine continues throughout the greater part of life. The oldest part of the enamel is its deepest part, where it is in contact with the dentine. Its surface was the last part formed. The oldest part of the dentine is that nearest the surface of the tooth. In fact, the dentine grows from without inwards, so that the part most recently formed is close to the pulp cavity. The enamel grows from within outwards, so that the enamel of most recent formation is that which forms the outer surface. These two structures at one period of development actually grow in opposite directions from the same neutral point where each commenced to grow.

Cementum.—With reference to the cementum, it should be remarked that this tissue is not formed until after much of the dentine and enamel has been produced—in fact, not until the tooth has increased to such a size that the surface of the dentine of the fang, or the surface of the enamel covering the crown, comes into very near relation with the cells upon the inner surface of the membrane which forms the tooth sac. It has been said that this membrane becomes itself ossified, but the changes occur in a tissue which is produced beneath it, and which in certain cases is formed in very large quantity. Although some forms of cementum closely resemble ordinary bone in character, important differences may be observed, both in structure

and mode of formation, in the teeth of man and many mammalian animals.

The view of Prof. Huxley that, in a morphological point of view, the cementum is homologous with the enamel, seems to me incompatible with the following facts:—

1. The cementum in the herbivorous tooth covers the enamel, and, in exceptional cases, it occupies the same position in the human tooth.

2. Its formation does not commence until the formation of the enamel is completed.

3. The character of the soft tissue (columnar cells) which precedes the enamel is distinct from that which exists before cementum is produced (tissue with stellate cells).

Of the formation of the so-called intercellular substance of dentine.—Intimately connected with the question of the nature of the dental tissues, is the question relating to the mode of formation of the so-called intercellular substance; for it is obvious that if it can be shown that dentine agrees in its structure with cartilage and bone, and consists of "*cells*" and "*intercellular substance*," it belongs to the series of *connective tissues*. If dentine is a connective tissue, without doubt it is formed beneath the line which corresponds to the position of basement membrane, and must be considered as a dermic and not as an epidermic structure.

Although in my earlier lectures I have advanced facts and arguments against this view of the structure of connective tissues, it is necessary for me to consider the matter here somewhat in detail, particularly as regards bone and dentine. And first, let me consider

how far the so-called wall of the dentinal tube, as distinct from the intertubular tissue, has a real existence. Those who maintain that the lacunal cell of bone and the dentinal tube of dentine possess special walls, seem to have overlooked the fact that the so-called "cells" of lacunæ and "soft contents" of the dentinal tubes become smaller and more contracted, or shrink, as the tissue advances in age. It, therefore, follows either that what at one time was *cell wall* must become at a later period *intercellular substance*, or else the cell wall must shrink in consequence of the deposition of new matter upon its *external surface*. If the first view is accepted there can be no necessity for distinguishing cell wall from intercellular substance. If the last is received, the cell wall must, as it shrinks, gradually become puckered, which is not the case. There would be, moreover, upon this view great difficulty in explaining how or why the calcareous matter passes through an old, condensed, and puckered cell wall to be deposited outside it.

The theory of the formation of intercellular substance as a process distinct from the production of cell wall is now generally received, but the advocates of the doctrine have met with terrible difficulties in the attempt to apply the theory in detail, and, like the supporters of many fanciful hypotheses, they avoid details which seem adverse to their favourite theory. This doctrine rests upon the most gratuitous hypothesis, that intercellular substance is deposited around and between cells. If such a deposition really occurred, it is surely reasonable to conclude that we ought to be able to find at least one example in nature in which such deposition was

unquestionable; but not one has been pointed out by the many supporters of this favourite but fanciful doctrine. Let the reader suppose, for example, a number of spores of mildew arranged at a short distance from each other in a gelatinous medium, holding in solution calcareous matter; let him further suppose that the calcareous matter was deposited between and around the several cells, he would then have a calcareous intercellular matrix, in which masses of protoplasm, each being surrounded by a distinct cell wall, were contained, and if he supposed the cells to have communicating processes, he would have a tissue much resembling bone. To some, such a theory may seem plausible enough, but let the reader further remember these facts:—

1. That in the formation of bone, cartilage, &c., the so-called cells are gradually becoming separated farther and farther from each other.

2. That up to a certain period they are increasing in size, and that after this they diminish in size.

3. That in ossification, the deposition of the calcareous matter occurs first in the very centre of the cartilage, not upon the surface of the cell.

4. That "intercellular substance" gradually increases as the tissue advances towards its perfect state, and that it exhibits differences in refractive power in the forms of lines around the cells, almost resembling laminæ in some cases.

It will be observed by any one who considers these points carefully, that they are incompatible with the supposition that the intercellular substance is gradually deposited between the cells.

Again, the deposition of this "intercellular substance," distinct from the cell wall and independently of the cells, involves one of the following suppositions:—

1. The existence of an analogous substance in the blood itself; or,

2. The possibility of the cell exerting some metabolic action upon, or converting the matter deposited from the blood into the peculiar and characteristic matter constituting the "intercellular substance."

All attempts to prove the first position have failed. The second supposition is opposed to broad facts. It is well known that various matters may be deposited upon the outer surface of cells, as crystalline matter may be deposited upon any foreign substance placed in a strong solution of the crystalline material; but there is no evidence whatever that the cell exerts any mysterious metabolic action upon them. The matters deposited here must be simply precipitated from a solution, the cell wall being merely incrusted with them.

I have shown in my earlier lectures that the so-called cell wall increases in thickness, not *by deposit upon its outer surface*, but by the successive deposition of matter upon its *inner surface*, so that it is caused to expand by distending force exerted from within. The outer part, or that most distant from its centre, is invariably the oldest. If intercellular substance is deposited *around* the cells, it must be shown either that it gradually and evenly increases in every part of its substance, or in the part midway between the respective cells only, or upon the outer part of the cell wall; but neither of these positions has been supported by facts.

The view involves, in fact, the existence of growth according to two distinct and opposite processes—the cell wall being increased by deposition from within—the intercellular substance being increased by deposition from without. The fact, that in many cases the so-called "cell wall" does not exist as a structure distinct from the "intercellular substance," and does not differ from it in chemical composition or properties, renders such a position untenable, since it is unreasonable to infer that two layers of matter, in all respects the same, and contiguous to one another, should be produced by antagonistic operations (deposition in a direction *from centres* and deposition *towards centres)*, while upon such an hypothesis, the objects fulfilled by the cells are not explained. If the cells take no active part in the formation of the intercellular substance, *why are they constantly present while this process is going on?*

It has yet to be shown that the formation of any tissue peculiar to living beings, proceeds in a direction with respect to the germinal matter, from *without inwards*, while there is not the smallest difficulty in demonstrating many instances in which deposition most assuredly takes place from within outwards. It is not in accordance with what is yet known to believe that so universal a process as *growth* occurs according to two such opposite and physically incompatible processes as *attraction towards*, and *evolution from*, a centre.

Hence, I cannot but feel that further investigation will demonstrate that the deposition of intercellular substance theory is erroneous.

Of the development and formation of the palatine teeth of the common newt.—I must not attempt to discuss the various changes occurring in the course of development of the mammalian tooth, for to do so, even cursorily, would occupy many pages, but I may, in few words, discuss the most interesting part of the question—namely, the mode of formation of the papilla. Now, in a minute and difficult inquiry like this, which involves an examination of some of the most delicate tissues at an early period of development when they are exceedingly soft, the observer endeavours to discover one example in which the various anatomical points are very distinct, and then he may, with the aid of the positive facts already ascertained, study higher and more complicated phenomena of the same kind with considerable advantage.

After examining the teeth of a number of animals at a very early period of development, prepared in the most careful manner for the purpose of investigating the nature of the earliest changes occurring in the formation of the papilla, I found that the process of development could be studied in its simplest condition with comparative facility in the palatine teeth of the common newt (triton cristatus). As young teeth are being continually formed in connexion with the mucous membrane of the upper jaw *of the adult animal*, their development could be investigated under great advantage. In the embryo the tissues around the developing teeth are as soft, or softer, than the dental papillæ themselves, and this renders the investigation exceedingly difficult; but in studying the process as it occurs in the fully developed newt, there is no such serious practical disad-

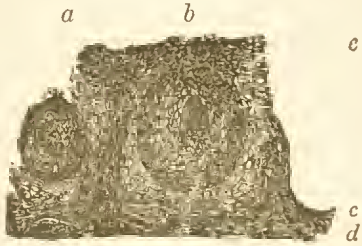
vantage. Moreover, the number of these teeth is considerable, and being situated in the central part of the upper jaw, they can easily be detached as they grow, with the mucous membrane itself. Sometimes ten or a dozen teeth, in different stages of development, can be isolated in a single specimen. The vessels of the mucous membrane can be minutely injected without difficulty, so that we can ascertain with considerable precision the exact relation of the capillaries to these teeth, and the follicles in which they are developed.

In investigating the changes taking place in the development of a tissue, great advantage will always be gained by studying the process as it occurs in the fully formed animal. It is a mistake to suppose that the process of development of tissue can be studied only in the embryo. Every stage of development of fibrous tissue, cartilage, bone, muscle, nerve, ganglion cells, fat cells, and many other tissues, may be seen in the fully formed frog, and the changes observed far more distinctly than in the embryo. In the adult newt the development of the teeth may be watched from the very earliest stages, and in the same animal may be demonstrated the changes which occur in the development of a complicated gland like the kidney, testicle, and ovary.

The very youngest palatine teeth can be detached from the surface of the mucous membrane covering the palate of the newt, and it is to be noticed that in attempting to remove the epithelium from the surface of the mucous membrane, a number of entire tooth sacs, many of which contain each an embryonic tooth, are often detached with it.

Now, each of these little "sacs" is an oval mass, consisting entirely of cells very closely resembling epithelial cells in their general character (Fig. 1). At this early period there is no actual *capsule*, or *external membrane*, but the most external cells are somewhat flattened and spread out, as shown in the figure. This flattening and spreading

Fig. 1.



Two very young tooth sacs, with developing teeth, from the palate of the newt (triton cristatus), magnified 215, and reduced to $\frac{1}{4}$; *a*, a very young tooth sac and tooth; *b*, another, a little older; *c*, marks the position of the basement membrane; *d*, capillary ramifying in the sub-basement tissue; *e*, the epithelial structure in which the tooth sacs are embedded. This lies upon the surface of the basement membrane *c*.

out evidently arises from the first cells formed being pushed outwards towards the circumference by the growth of new cells in the centre of the collection. These little collections of epithelial-like cells, which would be termed sacs, are

entirely surrounded by and seem embedded in the epithelium of the mucous membrane, and the cells at the summit of the sac are often seen to be uninterruptedly continuous with those outside. The cells* of which these collections are composed differ somewhat from those in which they are embedded. It need scarcely be said that neither these nor the cells external to them are ciliated. They are of a more oval form than the ordinary epithelial cells covering the palate. The general appearance of each collection of cells is such as would be expected to result if at an earlier period one epithelial cell amongst its fellows had increased in size, divided, and subdivided, and so formed a compact collection of cells in the substance of a cellular layer. At this time the entire mass is composed of small cells only.

The tooth itself is formed in the very centre of the oval mass composed of cells, after cell multiplication in this part has ceased (Fig. 1, *a* and *b*). As I have already stated, at this time the oval mass has no fibrous or membranous capsule. The most external cells are a little flattened, but after the tooth has become quite distinct, the entire mass may be broken up by very slight pressure, and nothing but cells result. Moreover, cells are formed to the extent of two or three layers upon the surface of the

* By the word "cell," as has been already stated, is meant an elementary part, consisting of a mass of germinal matter which, in the preparation, is coloured red with carmine, surrounded by a layer of soft formed material. Each of the little bodies which compose the oval mass sac, in the centre of which the tooth appears, and each of those around the sac (Fig. 1) is a "cell."

mucous membrane beneath these oval collections of cells. It is, therefore, quite certain that basement membrane can have nothing to do with the origin of these palatine teeth of the newt, and it is also certain that the young tooth is *surrounded on all sides by cells.* It is developed in the midst of cells. The dental tissue is formed by the impregnation with calcareous salts of a soft matrix, produced, as in other cases, by change occurring in the outer part of masses of germinal matter; and cells which take part in forming new matrix occupy the cavity of the shell of dentine, even when its formation is considerably advanced. No vessels are near the collection of cells in the midst of which the young tooth is growing, nor do they pass into the pulp until some time after the tooth has reached a considerable size, and the formation of the fang has commenced. The first part of the tooth which is formed is the summit, and the fang grows *downwards* from the epithelial surface towards the vessels, and the bone into which it is to be received.

The tooth is not developed from a papilla consisting of sub-basement tissue, but it is formed in the very centre of a collection of cells, and it is clear that these cells have been formed in the central part of a preëxisting cellular mass. So that the oldest cells, which seem but to perform the office of a protecting envelope, are outside, and as new ones have been produced in the centre, these oldest cells have been somewhat flattened upon the surface, thus giving the appearance of a boundary or an imperfect capsule, which enables us to distinguish these masses from the collection of cells in which they are embedded.

Next comes the important question, how do these collections of cells originate? I feel confident that they commence in a cellular mass, which, to all appearance, is an epithelial structure. I have seen a single cell differing from its neighbours, in its larger size, dividing to form three, or four separate cells, and I believe this was the original cell from which all those which constitute the collection in which the tooth at length appears, resulted.

The cellular mass is certainly uncovered by basement membrane (Fig. 1). It is so easily torn away from the surface of the fibrous tissue upon which it rests, that it is often destroyed in preparing it for examination.

The stages which occur in the development of these teeth may be represented as follows (Figs. 2, 3, 4, 5). Fig. 2 represents a small collection of cells embedded in the epithelium upon the free surface of the mucous membrane. As the sacs grow, they may become partially enclosed in follicles, by the growth of the mucous membrane around them, as shown in different stages in Figs. 3 and 4. A further stage of the process would bring about the very condition of things which occurs in the development of the mammalian tooth, the enclosure of the so-called papilla in a sac (Fig. 5). The palatine teeth of the newt, however, are not enclosed in a sac at any period of their development.

Fig. 2.

Fig. 3.

Fig. 4.

Fig. 5.

Diagrams to show the manner in which the "papilla," which takes part in the development of the tooth, is formed in the midst of epithelium, and how this "papilla" may be enclosed in a sac. It will be observed that the vessels do not come near to the tooth until its formation is considerably advanced. *a* is the layer of epithelium; *b*, a black line corresponding to the position of the basement membrane; *c*, vessel.

Now, it must be borne in mind, that at the time the so-called "papilla" of the mammalian tooth is formed, there is no basement membrane, there is no sub-basement tissue, there is no indication of a line of demarcation between the texture, which will eventually be *epidermic*, and that which is *dermic*. There is a time when the cells, from which the epithelium of the epidermis is to be developed, cannot be distinguished from those which take part in the production of the areolar tissue, vessels, and nerves of the derma or true skin. It is certain that an elevation or "papilla" occurs when a tooth is to be formed, but I think that in the *central part of these "papillæ,"* which consist of collec-

tions of cells, *new ones appear*, and that this process continues, until at last the tooth structure *commences to be formed in the last collection of cells in the central part.* I consider that the dental "papilla" is entirely composed of modified epithelium, developed from what might be termed an epithelial cell. The collection of cells afterwards becomes enclosed in its sac by the growth of the mucous membrane over it, as represented in Fig. 5.

So that at every stage of development, the cells which take part in the formation of the dentine, are above the position of the basement membrane, but as the process is generally described, these cells must be, from the very first, beneath it. We have, according to the view generally entertained, first, the epithelium upon the summit of the papilla, then the basement membrane, and next the sub-basement tissue, in which it is supposed that the dentine is developed. According to this view, when the papilla is being enclosed in the sac, there would be *above the dentine three layers of basement membrane* :—1. That of the papilla. 2 and 3. The reduplicated mucous membrane which rises up around it, and ultimately encloses it. According to my view, there never can be more than the two last, as shown in Fig. 5.

It seems to me, therefore, that both dentine and enamel must be looked upon as calcified epithelial structures, and I think they may be regarded as epithelial, in the same sense that a hair, or the cells in a glandular follicle, such as the sebaceous gland cells, or the sweat gland cells, or the calcified cells of the mantles of mollusca are regarded as modified epithelial structures.

The relation of the tooth sac to the proper dental tissues.—If the foregoing conclusions are correct, the relation of the tooth sac to the dental tissues is easily understood. It has been shown that the enamel is covered superficially by a *vascular* membrane. This vascular membrane is the modified tooth sac. It has been shown that both the enamel and dentine are formed from epithelium, and it has been remarked that the cementum, or crusta petrosa, is sometimes developed upon the outer surface of the enamel, as well as upon the dentine of the fang of the tooth. In the complicated molars of the large herbivora, as is well known, this cementum is formed in considerable quantity upon the surface of the enamel, and in some teeth the amount of the cementum is equal to, or greater than, that of the dentine and enamel together.

It is often said that the cementum is formed by the ossification of the tooth sac, just as bone is formed by the ossification of periosteum; but it has been shown that beneath periosteum a number of bodies resembling cells are produced, and that these are the agents directly concerned in the production of the osseous tissue. Although the fibrous tissue of the sac of the tooth does not normally undergo ossification, there can be no doubt that this, like many other forms of fibrous tissue, may become ossified. Here, as in the periosteum, there are upon the deep surface cell-like bodies which are slowly produced, and from these the matrix results which afterwards undergoes calcification. The germinal matter of some of these cells remains for a time as the "nuclei" of the lacunæ which are sparingly scattered through the cementum. The very

slow formation of this tissue, as compared with that of the enamel and dentine, is, doubtless, dependent upon the diminished proportion of nutrient matter distributed to the tissues as the tooth advances in development. In certain morbid conditions, a more rapid production of cementum is associated with increased vascularity of the so-called periosteum of the fang, which represents the remains of the lower part of the tooth sac.

Although I have not succeeded in demonstrating the "periosteum" of the tooth as a structure distinct from the "periosteum" of the bony socket, as Mr. Spence Bate maintains, there can be no doubt whatever that, however closely these two structures may come into contact, continuous ossification never takes place. The cementum, however closely it resembles bone, never becomes structurally continuous with the bone of the socket, while the formation of cementum sometimes proceeds to such an extent abnormally as to connect two fangs, or even two teeth together (see the figures of Mr. Martin's specimen, Tomes' "Dental Surgery," p. 445).

Explanation of the different views now held upon the development of teeth.—The different opinions now entertained by observers upon the development of the dental tissues and their relation to basement membrane, or to the position which such a tissue ought to occupy, are clearly shown in the following diagrams representing the tooth and its follicle.

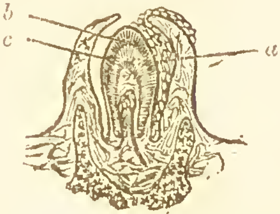
Fig. 6.

The basement membrane between the enamel and dentine. The view generally entertained.

In each figure *a* points to the black line which marks the position of the basement membrane, *b* is the enamel, and *c* the dentine. The bony socket is represented by the structure shaded with crosses; above are the soft parts forming the lips of the follicle, the epithelium of the surface of the mucous membrane being only represented on the right side. The vessels in the substance of the pulp are also represented in each diagram.

In Fig. 6 the black line is situated between the dentine and enamel. The enamel corresponds to the epithelium, the dentine to the connective tissue of a mucous membrane. This is the view entertained by most observers in the present day.

Fig. 7.



The basement membrane covering the enamel. Dentine and enamel being both sub-basement. The view of Huxley.

In Fig. 7 the black line corresponding to the basement membrane is seen to pass over the enamel, so that both the enamel and dentine lie beneath this structure. They are both dermic structures. This is the doctrine of Huxley.

Fig. 8.

The basement membrane *beneath* the dentine. The Author's view.

In Fig. 8 the black line is seen passing over the surface of the pulp beneath the dentine, so that both enamel and

dentine are regarded as modified epithelial structures. They are both epidermic. This is the view which I have been led to advocate from recent investigations.

Of the death of the tooth, and of caries.—Teeth, like some other tissues, may die and be cast off. The circulation in the vessels of the pulp being interfered with, the entire pulp dies, the blood corpuscles become broken down, and the coloured solution thus formed gradually stains the dentine. Still the tooth may be retained in its place for a long period of time, for although the pulp and surrounding dentine are dead, the cementum deriving its nutriment from the vessels distributed to the bone of the socket still retains its vitality, and oftentimes increases considerably in amount. If, however, the opposite process occurs and absorption takes place, the tooth soon falls out. Now, it would be said that when the vessels of the pulp are destroyed, and nutrient matter no longer permeates the tooth structure, that the entire tooth is dead; but it is doubtful if in such a case the enamel, the outer part of the dentine, and the inner part of the cementum, are more inanimate than when the tooth formed an integral part of the living body, and was supplied with nutriment from the same living blood as the soft parts. The tooth, although dead, remains firmly attached to the living parts, and continues to perform its important functions, like those hard organs which are connected with various parts of the surface of insects and crustacea. A dead tooth may remain for years, perhaps, firmly fixed in the socket, and it has recently been proved by the highly interesting researches of Dr. Mitscherlich that teeth which have been

removed from the body, even for years, may be fixed in the alveolus of a living person and retained there for a long period. In this case the tooth is not renourished, but remains as lifeless as it was before. It appears that by the agency of some of the cells of the periodontal membrane remaining in the socket, little cavities are formed upon the surface of the old cementum and dentine, and that afterwards new cementum is produced as a counterpart, and thus the dead tooth is firmly held in its place. Dr. Mitscherlich's paper, which contains many things of physiological interest, has been translated and published in Truman's "Archives of Dentistry," No. II.

Of caries.—There are few subjects which have been more carefully studied than caries; but we have yet very much to learn with reference to the exact nature of this morbid process. That the dentine becomes very soft, owing to the removal of its calcareous matter, is a fact known to every one; but how this change occurs, and the precise circumstances which determine it, are still unknown to dentists and physiologists.

Oftentimes low vegetable organisms may be detected in the carious matter, and by some, these have been supposed to be the cause of the disease; but fungi will invade any tissue which is in a softened state and not permeated by the normal fluids. Such fungi grow in vast numbers in all the old epithelial cells upon the surface of the mucous membrane of the mouth, and if the deeper cells suffer in nutrition, they often become invaded by such fungi; not only so, but the minute germs of such simple vegetable organisms exist even in the soft tissues in the

interior of the body, and they germinate if the conditions become favourable—that is, if changes take place in the normal tissue whereby its integrity is destroyed, or in consequence of which its death results. With reference to the nature of caries two views are entertained; one, that the change depends merely upon the action of the fluids of the mouth; the other, that some alteration in the nutrition of the tissues precedes the morbid change. Mr. Tomes has shown that the mucous membrane under irritation pours out a fluid capable of injuring susceptible teeth. That the fluid which acts possesses an acid reaction has been shown by experiment; but it is doubtful if, at least in the majority of cases in which the disease occurs, there is not a predisposition to it. The enamel and the dentine are the tissues usually affected, and the change goes on much more rapidly in the dentine than in the enamel. According to Mr. Tomes, the central portion of the enamel rods is that which is first attacked. In the case of the dentine, the intertubular substance is the first to go.

Now, as I have already shown, this intertubular substance is formed before that portion of dentine which constitutes the "wall" of the dentinal tube; and the oldest part of this intertubular substance is that which lies just beneath the enamel,—a part of the dentine in which caries very often commences. The dentine here is situated farthest from the nutrient vessels, and in cases in which any defect in formation had occurred, this would be the portion to undergo change. It is quite possible that in many instances the dentine in this situation may have been imperfectly formed during the early period of development,

or the calcifying process may not have been properly carried out. These circumstances render the dentine very liable to disintegration if exposed to the action of acid fluids, or to saliva which was not perfectly normal. Perfectly sound tissue would resist the action of fluids which would certainly cause destruction of imperfectly developed dentine. The dentine is probably permeated very slowly by fluids which pass through the vascular walls from the alkaline blood. In the normal healthy state these alkaline fluids gradually pass from the pulp towards the outer part of the tooth; but if from any cause the currents flowing in this direction cease, the fluids of the mouth may attack the surface, and thus give rise to caries.

Although in this way local actions may alone determine caries, it is probable that in almost all the cases in which it occurs, there is some defect in the formation of the dentine which renders it predisposed to decay; not only so, but caries is often associated with some temporary derangement of the health. That form of dyspepsia which comes on from mental anxiety seems, in some cases, to be intimately connected with the destruction of the dentine from caries. Nor are the dental the only tissues the nutrition of which is affected under these circumstances. Mental anxiety seems to be a cause of many chronic diseases. Some suppose that this arises from a peculiar and direct action of the nerves upon the process of nutrition; but it is much more probable that this influence is indirect, that the derangement of the digestive process and the action of the liver lead to changes in the composition of these nutrient fluids, and that in this way the results we have

been considering are caused. Those tissues which exhibited any imperfections of structure or composition would be the least able to resist the deleterious influence which must arise from such changes in the composition of the fluids by which they were permeated.

LECTURE X.

ON LIFE.

And now, Gentlemen, I come to a part of my subject which I feel myself incompetent to consider. Yet I would not willingly omit all reference to the question of the nature of life in these lectures. This most abstruse and difficult subject has been very freely discussed of late in many works intended for public reading, and has engaged a large share of attention. It would not, therefore, be right in me to pass the matter over. Moreover, it is certainly true, and the remark applies even to those who are most determined to avoid mere speculation, and endeavour, as far as possible, to be influenced only by the results of observation and experiment, that the thoughts will sometimes stray, perhaps against the will, into distant and speculative regions. Nor am I sure that the chief reason why science is becoming so popular is not that the mind of a well-educated person, after a certain time spent in discipline and training, may delight itself by wandering in that region which connects the known with the unknown, where the most thoughtful of every age have found subjects for never ceasing contemplation, and where the human intellect may exercise without restraint its highest

faculties. I may be permitted to recount briefly the general inferences which seem to me justified by observation, and to give a brief outline of the views I have been led to entertain upon this most difficult question; and I am the more desirous of discussing this matter because it so happens that my conclusions are opposed to those generally entertained and taught by contemporary scientific men.

In this course of lectures I have shown that all discussions with reference to vital actions must be restricted to the consideration of the changes which take place in the particles of germinal matter only, for here the inanimate matter certainly becomes living, and after retaining for a time the active power of animating new matter, the particles most distant from the centre where they became living lose all vital power, and become resolved into various substances, which, there can be no doubt, are again under the influence of physical and chemical laws.

I attribute these changes to the influence of a peculiar power, which may be called vital power, and feel compelled to accept an hypothesis, inconclusive though it be, until a reasonable explanation of the phenomena under discussion is offered. It is now four years since I advanced arguments in favour of the view which I have been led to entertain. My doctrine has, it is true, met with some opposition, but its opponents have not discussed the questions involved. They simply deny the existence of vital power, and scrupulously avoid all discussion regarding the nature of the phenomena which are attributed by me to its influence.

We are able to investigate the composition of matter before it becomes living, and we can study the forces which are in relation with it. So, also, we have learned much from the wonderful advances of organic chemistry during the last few years, of the nature of the chemical compounds which are produced when germinal matter becomes formed material, and when formed material is disintegrated by the action of water, oxygen, and other substances.*

We know something, too, of the compounds resulting from the sudden or slow death of germinal matter.

But we know literally nothing of the relations existing between the different elements which constitute a particle of *living germinal matter.*

Between the time that the inanimate pabulum becomes living and the time that the living matter becomes formed material, there is an interval in which the matter exists in a very peculiar and exceptional state. *This is the living state—a state which is to be distinguished from every other state in which matter is known to exist*—a state not determined or caused by external circumstances, not capable of being communicated to matter through space, nor of being excited in matter by any known agents or combination of circumstances—a state which may cease to be manifested at any moment, but which, as far as is known, cannot be caused to commence anew. Now, those who have dis-

* For the evidence in favour of the view that the *germinal* or *living* matter does undergo conversion into *formed material*, as *cell wall, intercellular substance, &c.*, see Lectures I., II., and III.

cussed the nature of vital forces, have not alluded to this temporary state. They have restricted themselves to the consideration of the matter *before* it assumed this *living* state, and after it had passed through it.

I have shown that every particle of matter exhibiting *vital phenomena* is derived, not from the formed material, but from preëxisting *living* or *germinal* matter, which exhibited similar phenomena, and so from the first creation. This living matter is always colourless, always contains much water, and consists of particles, which, when free, invariably become *spherical*.

It may be remarked that lifeless matter may exhibit many different forms, and occurs in a variety of different states, but the living matter of the different beings in creation always exhibits the same general characters. I have adduced facts which, I think, justify the conclusions that the spherules of which the living or germinal matter consists are composed of spherules *ad infinitum*—that the intervals between them are occupied by smaller ones separated from each other by fluid which contains in solution—1, matter about to become living; 2, substances which do not necessarily form a constituent part of the living mass, and which are not capable of being animated; and in very many cases, 3, substances resulting from the changes ensuing in particles which have arrived at the end of their period of existence, and the compounds formed by the action of oxygen upon these.

I believe that all these spherical particles are free to move in fluid, and that the movements in all living particles take place in the same direction—from the centre at

which the particles became living,—*centrifugal.* The smallest living particle must be of complex composition; but how the elements are related to each other, how they are influenced by their forces, or whether they affect or are affected by matter at a distance from them, there is no evidence to show. It seems to me probable that the ordinary forces of the matter of which the active living particles are composed are in abeyance. The changes which occur cannot be explained by physical and chemical laws. The matter before it becomes living exhibits certain well-known properties. The formed material produced exhibits totally different properties, and the disintegration of this formed material gives rise to the manifestation of force in the shape of work performed; but while the matter *lives* actively the most wonderful changes of place and chemical decompositions of new matter are silently and imperceptibly taking place, and these changes may be communicated to new particles of matter, and so on for ever, or the changes occurring may suddenly and abruptly cease, in which case they can never recur in those particular particles or masses of matter. It need scarcely be said that such phenomena are not known to occur in inanimate matter.

Particles which are lifeless attract one another, and in many cases act upon each other, producing compounds which exhibit well-defined characters. The living particles seem neither to attract nor to repel each other, but they possess the power of moving from the centre at which they were produced. The arrangement of the elements in the living particles must be totally different to that which existed before the matter became living, for all living par-

ticles, however they may differ in chemical composition and properties, exhibit the same form, and behave towards certain reagents in precisely the same manner.

Does not all this indicate that the ordinary physical and chemical forces of matter are in abeyance while matter exists in this temporary *living state?* It seems as if there existed at this time a power in obedience to which the matter became affected in a manner we cannot explain. It is this power which we understand as the life. It is in obedience to this power that the living particles move *from* centres instead of gravitating *towards* centres, like the particles of ordinary matter. Nor can these centrifugal movements be accounted for by any physical laws yet discovered.

VITAL MOVEMENTS.

Perhaps the spontaneous (?) movements observed during life in many forms of living matter from different living beings are among the most simple of vital phenomena—simple, as, for example, when compared with the wonderful chemical changes which take place, or with the marvellous actions which result in the production of a special tissue with some special property, as, for instance, that of contractility. Perhaps of these movements the most simple are such as may be observed in the common amœba, or in the pseudopodia of foraminifera, or in the white blood corpuscle, pus corpuscle, or mucous corpuscle. In these cases a part of a mass of matter, the general form of which may be spherical, moves in advance of the general mass, and then perhaps

becomes again incorporated with it, or it may move away to a considerable distance and then be detached. Such movements may occur in every part of the mass, and may be seen at opposite points of the circumference at the same moment. Particles which at one moment may be on one side, the next may pass over to the opposite side. Now, these movements have been accounted for by endosmose, by diffusion, by electricity, by an inherent power of contractility (whatever this may be), by the attraction exerted by surrounding matter, by the influence of the nucleus (not explained); but not one explanation has been offered which can even be looked upon as plausible. The movements themselves have been but very imperfectly considered, and movements of several kinds essentially different from one another have been included under the same head.* We shall find that the more carefully and minutely we investigate this apparently very simple phenomenon, the more inscrutable it will appear to us. It is obvious that if one part of the mass is pushed onwards by another part, the process of pushing has yet to be explained. But any part may advance before any other part. It is certain that gravity has no influence, for the particles move quite as quickly from as towards the earth. A living particle suspended in fluid often germinates by producing branches radiating from it in every direction. Living matter cannot be termed a colloidal form of matter, because it is not in the same state in every part. The continual variation in composition and

* See a paper "On Contractility, as distinguished from purely Vital Movements."—*Microscopical Journal*, July, 1864.

in position distinguishes it from every other form of matter.

Many facts I have advanced show conclusively that there is a general tendency in the particles of every mass of living matter to move in a direction from a centre, while the pabulum moves towards the centre. Suppose we assume that the particles of which a moving mass is composed consist of particles every one of which exhibits the same tendency to move from centres. We know that in a mass of living matter are spherical particles varying much in size, and it seems not impossible that the varying intensity of invisible movements in the different component particles may cause the movements which we observe in the mass of germinal matter. The particles being all free to move in fluid, some would move in advance of others. Nor is it possible to conceive that a mass constituted as above described would ever come into a state of equilibrium, because every particle is undergoing change, and at a different rate at every moment of its existence. New particles are being formed, old ones are dying, and being resolved into new materials. You ask me what causes these particles to move thus? I can only answer LIFE; and I am further led to the conclusion that the influence of this mysterious agency upon the movements diminishes as the particles move farther and farther from the centre, until at last it ceases. The particles *die*, and then their component elements come again under the influence of ordinary forces. Such a theory involves the supposition of an *inherent tendency of the particles of living matter to move from the centre at which they became living, that*

is, in a direction the very opposite of that in which lifeless particles would move. This is the hypothesis which I venture to advance, and which is supported by many broad facts alluded to in these lectures.

CHEMICAL CONSTITUTION OF LIVING MATTER.

I am led to conclude that all chemical forces are likewise in abeyance. We cannot say living matter is composed of this or that substance, for we cannot subject it to chemical examination. What we test is not the living matter, but the substances resulting from its death. It is certain that all living matter contains much water, but how this water exists we have no evidence. We know that when it dies we can obtain water, but then we can obtain salts, and we can obtain a matter allied to what is called fibrin, which becomes solid spontaneously, and shrinks of its own accord into a smaller space than it occupied when it was first produced; and we can obtain another substance dissolved in water which resembles what we call albumen. But it would be absurd to say that the living matter was composed of fibrin, albumen, and salts, dissolved in water; and it is most probable that the elements of the water itself may exhibit some exceptional relation to the other elements of which this living matter is constituted. It is remarkable that every kind of living matter by immediate death becomes resolved into very much the same kind of substances. Fibrinous, albuminous, fatty (perhaps amyloid),

saline matters, and water;—while, if the particles are allowed to die in the organism very different compounds result, according to the different conditions under which the masses of living matter are severally placed. You must not infer that I consider that all forms of living matter consist of the same elements, for it is certain there are differences not only in the elements present but in their relative proportions. Still there are characters in which all forms of living matter agree, although the results of their living are so very different. All living matter is colourless, structureless, formless; all possesses inherent power of movement, of decomposing certain substances which form its pabulum, and of causing their elements to occupy some peculiar relation to one another; and by death, every kind of living matter becomes resolved into the same classes of substances chemically speaking. During this living state I believe the elements of the matter and the forces associated with them are maintained in some remarkable and exceptional condition which is quite peculiar, to which no parallel whatever can be offered, and I attribute this to the operation of VITAL POWER. This vital power is not ordinary force, nor anything that can be rendered evident to the senses. Not one of the very simplest of the phenomena called vital can be explained without admitting its operation. For instance neither chemist nor physicist, nor the two combined, can explain the formation of organic matter so low and simple as the envelope of the common yeast plant; far less produce it artificially. Nevertheless, some consider it probable not only that simple organic matter will be pro-

duced in the laboratory, but that the matter so formed will give rise to other matter like itself, and this to more,—in short, that man will some day succeed in making an organism out of lifeless inorganic materials. I am not aware of any chemical facts which justify in any degree the position which has been assumed by some in the discussion of this question. No chemist has ever prepared a compound which will afterwards prepare more matter like itself from crude substances without the chemist's interference. And yet the simplest living matter does this, and much more than this.

THE PHYSICAL THEORY OF LIFE.

Several attempts have been made during the last few years to show that there is no essential difference between the changes occurring in living beings and those which take place in inorganic matter. These efforts have been so far successful as to induce many scientific men to acknowledge the importance of the views advanced, while some have even given their assent to the dictum that vital force is physical force, and have not failed to assist in propagating it.

That chemical changes occur in living beings closely resembling those which take place under certain circumstances in inanimate matter, and that from the action of certain substances upon each other, whether in the body of an animal or in the laboratory of the chemist, the same definite compound may result, is admitted by all;

but this is a very different proposition to that which asserts that the phenomena accompanying the changes in the inanimate matter forming the earth's crust are the same in their essential nature as those which are associated with the formation and development of a living being.

It is true that physical and chemical changes are concerned in the building up and breaking down of every living tissue, but does it therefore follow that the *formation* of the tissue is the effect or consequence of these changes *alone?* It is undoubtedly easy to show that many of the changes occurring in inorganic matter resemble changes which take place in living organisms; but it is surprising that many devoted to physical science, who have scarcely acquainted themselves with the physiological bearing of the question, and have only considered the phenomena as they occur in the fully developed man or animal, should have gone so far as to assert that *all* the changes were due to physical and chemical actions alone. When we come to a very careful examination of the phenomena in their simplest condition, as manifested in a single cell, the remarkable differences which really exist between physical and chemical, and *vital* actions present themselves in a sufficiently striking form to convince the mind of their essentially distinct nature. But in these days there is little prospect of the phenomena occurring in a single cell being regarded with much interest. The formation and destruction of faunas and floras, asteroids and worlds, suns and systems, absorb the attention.

The very terms formerly applied exclusively to the changes occurring in living things are now used in speak-

ing of lifeless bodies. The willow leaf-like bodies in the photosphere of the sun at a temperature sufficient to convert many metals into vapour, are "*organisms*" which "*develop*" and "*elaborate*" heat and light from the bosom of a non-luminous fluid (Sir John Herschel, "Good Words," 1863, p. 282.) These "organisms" have been compared to certain well-known forms of diatomaceæ. Nay, Dr. Tyndall speaks of a watch as a "*little creature*" which shows "*signs of animation*," and is "*restored to life*" by the application of its key! When philosophers speak thus, it is not to be wondered at that students should be led to the conclusion that vital and physical forces are one and the same in kind and essential nature, and that there is no real distinction between a mechanism made by human hands and a mechanism resulting from changes occurring in a living organism. Such terms are, perhaps, employed only metaphorically, and are not intended to be accepted in a literal sense. Still they are open to much misconception, and without doubt give rise to very erroneous conclusions.

At the same time I would remark that, while I am fully convinced that *vital*, as distinguished from physical force, exists in all living matter, I might go farther than many of those who adopt the physical theory of life, and admit not only that muscular and nervous action, but that the production of many of the compounds found in the secretions and in the blood are due to physical and chemical changes alone. I would admit that many of the phenomena which are now generally considered to make up "the life" of the fully-formed organism are

physical phenomena. But how very much there remains, nevertheless, to be explained! Of this any physicist would be convinced were he to spend but a short time in simply *observing* the changes which take place during the life of the simplest living thing. The phenomena upon which some physicists dwell are but the consequences of prior changes, which changes are of a very complex nature. The physicist does not inquire how the matters which are decomposed were produced. He regards their *formation* as nothing. They are there, and that is sufficient for him. He traces matter and force into a fully developed organism, and obtains matter and *work* from an organism, and this to him seems to be all that is worth inquiring about. He affirms that the organism is formed or built by the sun. He seems to think that pabulum goes into a living thing, and becomes changed chemically, just as it may be changed in his laboratory, and the results of this change are work and certain new compounds which are got rid of.

Yet how widely different are these conclusions from those which are arrived at from an actual investigation of the phenomena as they occur in living things, from which we learn that the inanimate pabulum, or certain of its elements, passes through a certain transitional stage in which very peculiar actions take place. The subsequent phenomena could never have occurred unless the matter had passed through this prior stage: everything which occurs afterwards is a consequence of the state of things existing at this period. Now, what has the physicist done towards the elucidation of the phenomena occurring in this state? Absolutely nothing! And not only so, but

he has ignored it as if it did not exist. To him there can be no phenomena occurring in living beings which are not of a nature identical with those occurring in the external world; so he abstains from investigating any of the phenomena which occur in living organisms, save those which take place in matter that has really ceased to live. Then he argues that, as all these phenomena, which he has shown to be purely physical, were until recently considered as purely vital, therefore all the phenomena of living beings must be physical. Nor does he even hint at the possibility of the existence of any other phenomena in living beings than those to which he refers.

Now, no one knows better than the physicist how very inexact and imperfect our knowledge even of the physical phenomena of living beings really is, and how very much yet remains to be discovered before we can explain that apparently very simple phenomenon—muscular contraction. One would have concluded, therefore, that physicists would have exercised the utmost caution in drawing inferences respecting the nature of the more abstruse and complex phenomena of living beings. No one knows better than the physicist that the force of muscular contraction very far exceeds that which can be obtained from any known arrangement containing the same weight of matter. The physicist prides himself upon never advancing to a second position until the first one has been clearly established. His mind must not be allowed to indulge in crude fancies but must be permitted to reason upon the results of rigid and exact experiment only, and

yet, no sooner does he, pass from his own special department to enter upon the consideration of the forces of organic nature, than he abandons the principles of investigation laid down, allows his fancy to indulge in the wildest theories, and puts forward as rigid facts what his sober reason would tell him are but the most vague and ill-defined assumptions.

Nor can it be denied that some of the disciples of the new philosophy, not content with the slow advance of real earnest research, have adopted the very old system of dogmatising. The first article of the new faith is that the *only* forces in Nature are derived from the Sun. Then, as all vital are natural forces, therefore vital force is but solar energy, and so the Sun is the source of all life. This dogma being accepted it is easy to convince people that in the production of higher and more elaborate structures, a greater amount of solar energy must be absorbed and rendered latent, than in the formation of very simple living organisms. It is admited by all that the comparatively simple vegetable structures directly absorb inorganic elements and solar energy, while animals can only take in matter and force which has been first elaborated by the vegetable kingdom. And since it has been shown (assumed?) that in the formation of a complex cell with high endowments a much greater amount of force is required than in the production of a simple cell, it ought to follow as a corollary that by the death and destruction of one of the brain cells of man, for example, a much greater quantity of force is set free in one form or other. than escapes at the death of an inferior structure. The

disciples of the new school having assumed that the brain cell in its formation absorbs a greater amount of force than a cell of lower organization, argue that the most highly endowed brain cell must have absorbed more force than an ordinary cell of the same character.*

Every one knows that a picture, a steam engine, a lifeless plant, animal, or man, is the result of the action of something more than ordinary force. And there is this obvious difference between the *lifeless* animal or man and the steam engine, that whereas the latter can always be made to work, there are no means of causing the former to resume work after it has once stopped, and yet a skeleton has been compared to a steam engine with the *fires out!* The results of the action, in the production of tissue, of the something more than mere force have been made to stand for the something itself. So the processes of disintegration and chemical change occurring in *lifeless* matter, the direct result of prior changes occurring while the matter was yet alive, have been regarded as the *life* itself.

It would seem rather that the marvellous endowments of a cell have nothing whatever to do with ordinary force. The liver cell does not differ, as far as is yet known, from the nerve cell in the different amount of force it contains,

* It might be further argued that, since in a great picture which results from the working of such highly endowed cells, must be accumulated a far greater amount of force than in a daub, it ought to follow that when the work of a great artist is subjected to combustion, more energy in the form of motion, heat, or light should be set free, than from the oxidation under precisely similar conditions of the same amount of oil, paint, and canvas in a crude and formless state!

but in the power resident in that part of it which consists of living matter. Some seem to ignore everything that cannot be put into a bottle or exhibited upon a screen, and naturally deny the existence of *power* as distinguished from *force*.

But is it not easy to show the fallacy of the views which are now very generally entertained upon this question, unless the truly *vital* are carefully distinguished from all other actions of living beings. If the two distinct classes of phenomena, to which I have many times adverted, are confused together under the term *vital*, it would be difficult indeed to refute any theory of life that has been or may be propounded, if but very moderate ingenuity be employed in arranging the terms in which it is expressed; but if these phenomena are different in their nature—and I think from the evidence I have adduced you will admit they are different—then the vital actions must be placed in a distinct category, and cannot be confounded with, or included under, physical phenomena.

I am quite unable to define the nature of the supposed vital power, but I think I have shown that the phenomena, which may be observed by all, cannot be explained, unless they are regarded as resulting from the influence of some peculiar power or agency upon ordinary matter and its forces. This power is, in its nature, as different from the force as it is from the matter. It is one of the immaterial agencies in Nature, the existence of which has been admitted by philosophers of every school and by the disciples of every faith, save by those few per-

sons who have embraced the dogma that in Nature there exists nothing but matter and force, and who profess to believe that the formation and action of the simplest organisms, as well as the working of the human intellect, are to be explained by the operation of material forces alone. Every one, however, who is a simple student of Nature, whether he regards her operations from a general point of view, or penetrates to her inmost mysteries, soon arrives at the conclusion that there is in all living beings something besides mere force and matter. True, he finds in living beings only the ordinary elements of matter, and he demonstrates the action of ordinary force, but he discovers that even in the lifeless matter from organisms, the elements are combined in a peculiar and subtle manner which he can imitate in very few instances, and he finds force producing results which are immeasurably beyond the results which the power of man can produce by directing the same forces. There seems to be something which controls the matter and directs the force, and this something acts in a peculiar and marvellous way, so that where work is required, this work is performed by *self-made mechanism*, without that waste of material and waste of force which occurs in the construction and working of every machine made by man. The amount of work produced by the expenditure of the same quantity of material is in fact many times greater than can be obtained in the most perfect machine, to say nothing of the unexplained marvel of the self-manufacture of the machinery, its constant repair, and the endless production of new machinery equally perfect and equally

powerful with that first formed. This something, which we may call vital power, or essence or spirit, or by any other name, influences the formation and action of every kind of living thing, from the simplest to the most complex. The production of the cell wall of the despised fungus cannot be accounted for without supposing such power any more than the complex mechanism of the human brain and its marvellous actions.

The figure below may, perhaps, enable me to explain with greater clearness than I have been able to do in words, the phenomena which I think occur in the smallest particle of living matter,—for example, the most minute vegetable sporule which appears under a power of 10,000 diameters as a mere point. It will also represent what I believe takes place in the ultimate particles of every form of living or germinal matter.

The most minute living particle.

In the central part are spherules which have recently assumed the living state, consisting of matter which was but just before inanimate pabulum. Beyond these are older and larger spherules which are still absorbing pabulum and growing. In many of these latter new centres are being developed. In all these VITAL phenomena are going on. As the particles move further from the centre, they undergo changes of another kind. They gradually cease to manifest VITAL phenomena. They lose the power of animating lifeless matter, and become resolved into passive formed material. This is represented in the drawing by fine lines. The formed material itself *is changed* by PHYSICAL and CHEMICAL actions. It may undergo condensation as it accumulates, or it may gradually become resolved into new substances of simpler chemical composition by the disintegrating action of oxygen, moisture, &c.

INDEX.

Dublin: Printed at the Medical Press Office